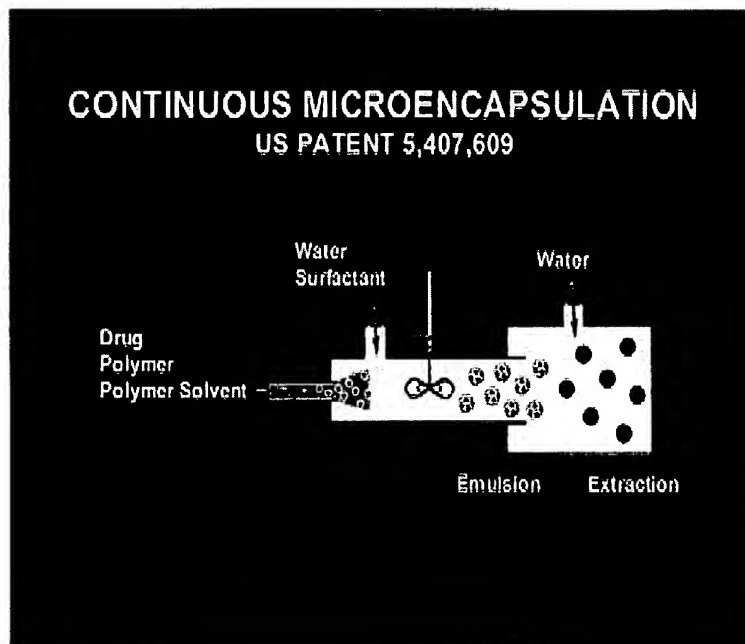




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Application No. 10/823,435  
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### Advantages

- US Patent issued 1995
- Fast encapsulation time -- milliseconds
- Minimal exposure to polymer solvent
- High encapsulation efficiency
- Good Yields
- Makes small microparticles  
<100 micron <10 micron

### Drugs Microencapsulated

- Proteins
- Peptides
- Small molecules
- Water-soluble drugs
- Hydrophobic drugs
- Drugs encapsulated in  
lactide/glycolide polymers

Figure 1

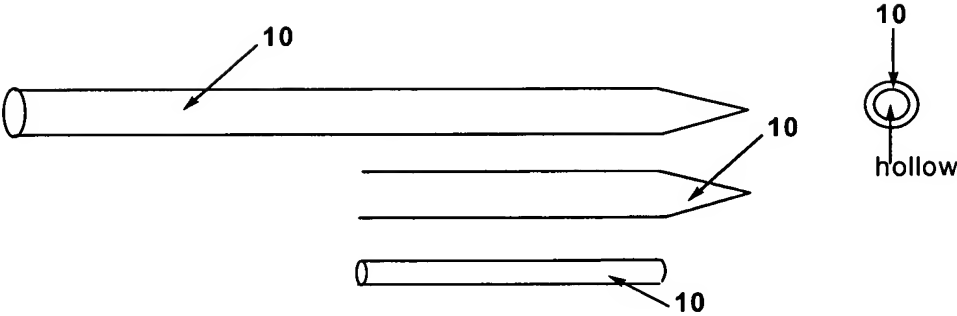


Figure 2

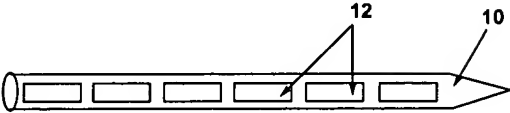
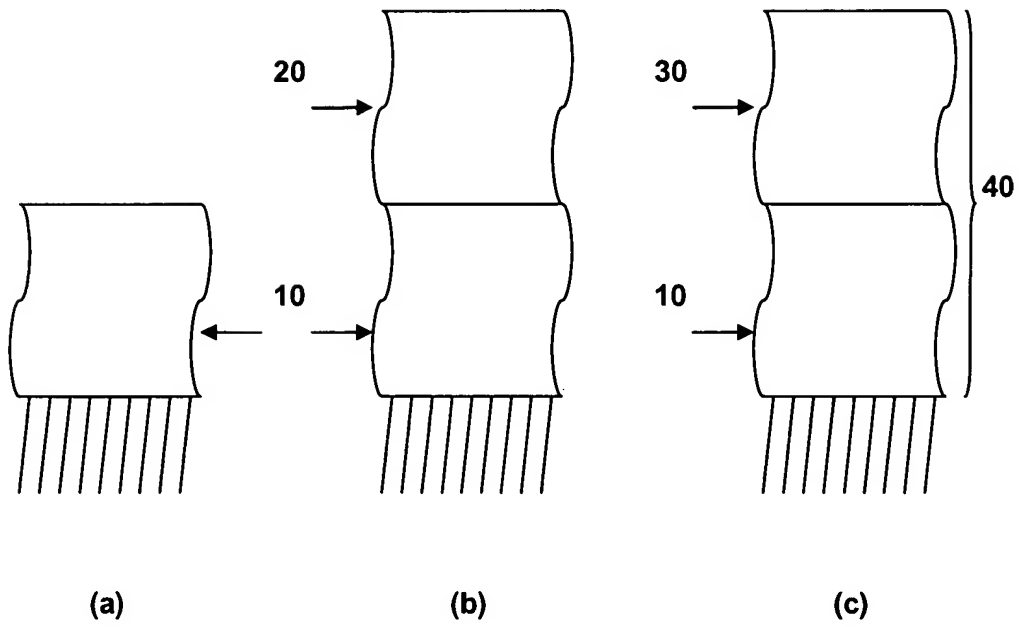


Figure 3



**Figure 4**

Conditions: Ambient

<b>Material:</b>	PX510	PX261	PX749	PX125	PX510 + 14% Paclitaxel
<b>Hardness:</b>	F	B	3B	4B	F

Conditions: 5 minutes in 37°C pH 7.4 Saline Buffer

<b>Material:</b>	PX510	PX261	PX749	PX125	PX510 + 14% Paclitaxel
<b>Hardness:</b>	F	B	9B	<9B	F

Hardness Rating: 2H-H-F-HB-B-2B-3B-4B-5B-6B-7B-8B-9B

Harder ←————→ Softer

**Figure 5**

Conditions: Ambient

<b>Material:</b>	PX510	PX261	PX749	PX125	PX510 + 14% Paclitaxel
<b>Resistance To Cracking</b>	< 3 mm	< 3 mm	< 3mm	< 3mm	<3mm

Conditions: 5 minutes in 37°C pH 7.4 Saline Buffer

<b>Material:</b>	PX510	PX261	PX749	PX125	PX510 + 14% Paclitaxel
<b>Resistance To Cracking</b>	< 3 mm	< 3 mm	< 3mm	< 3mm	< 3mm

**Figure 6**

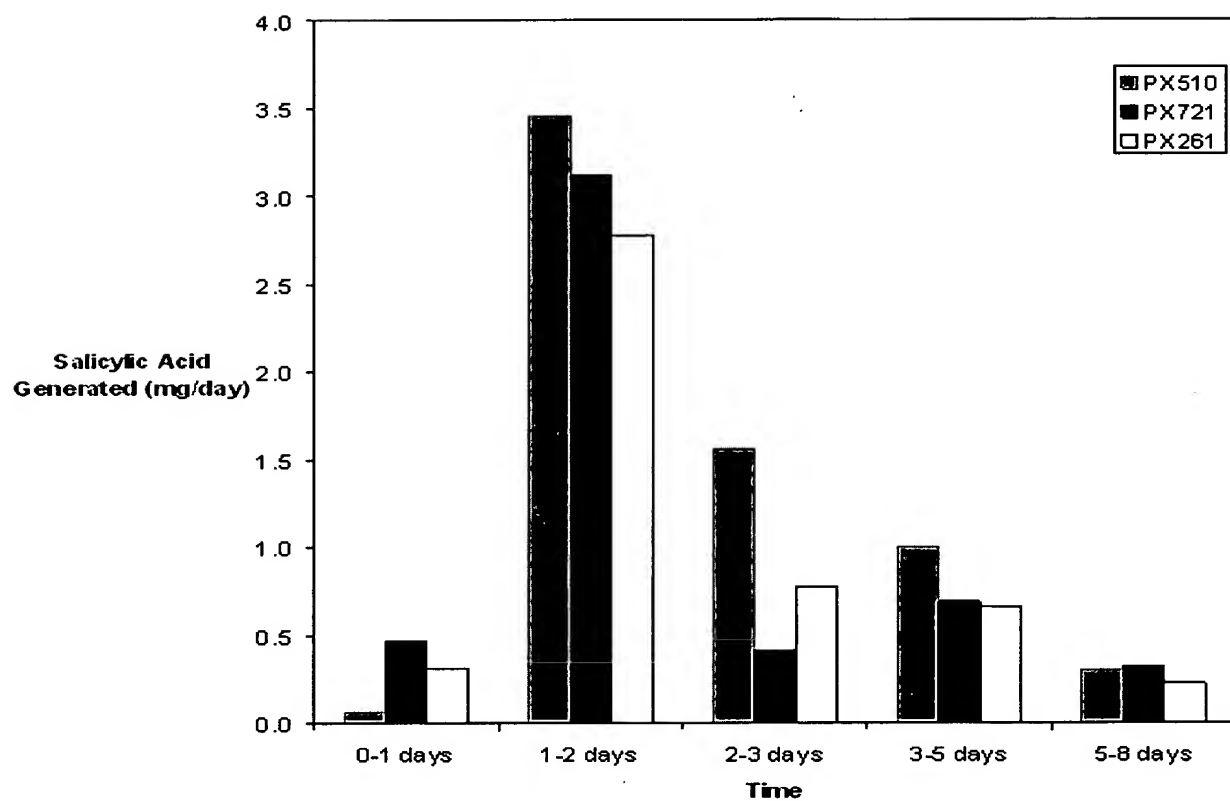
Attorney Docket No. 04271500  
Application No. 10/823,435  
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Conditions: Ambient

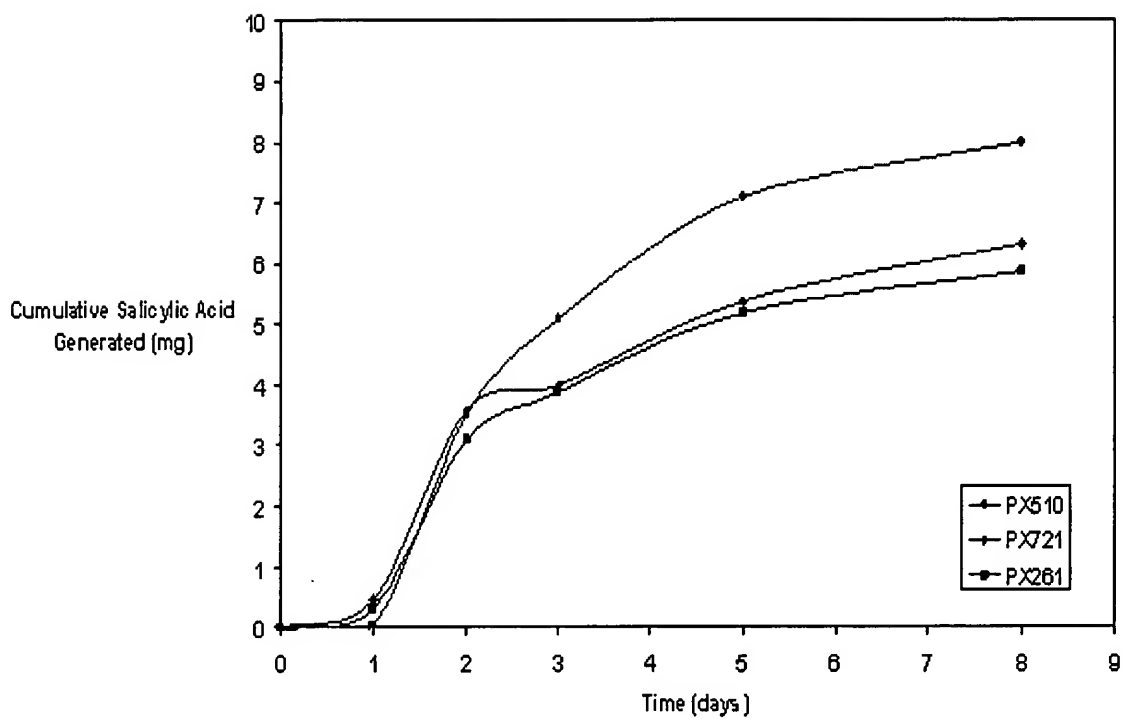
<b>Material:</b>	PX510	PX261	PX749	PX125	PX510 + 14% Paclitaxel
<b>Class:</b>	5B	5B	5B	4B	5B

Class Rating: 5B = 0% of coating removed from substrate  
4B = Less than 5% of coating removed from substrate

**Figure 7**

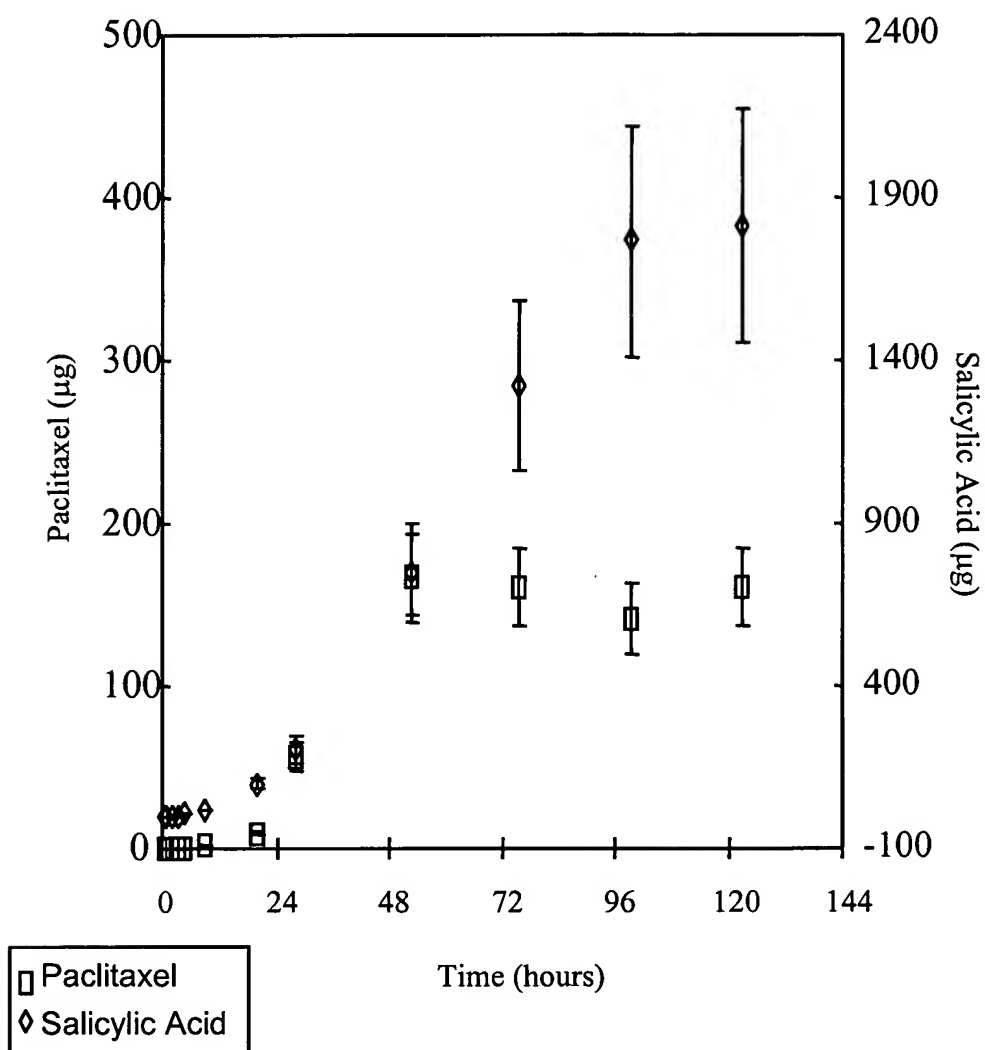


**Figure 8A**

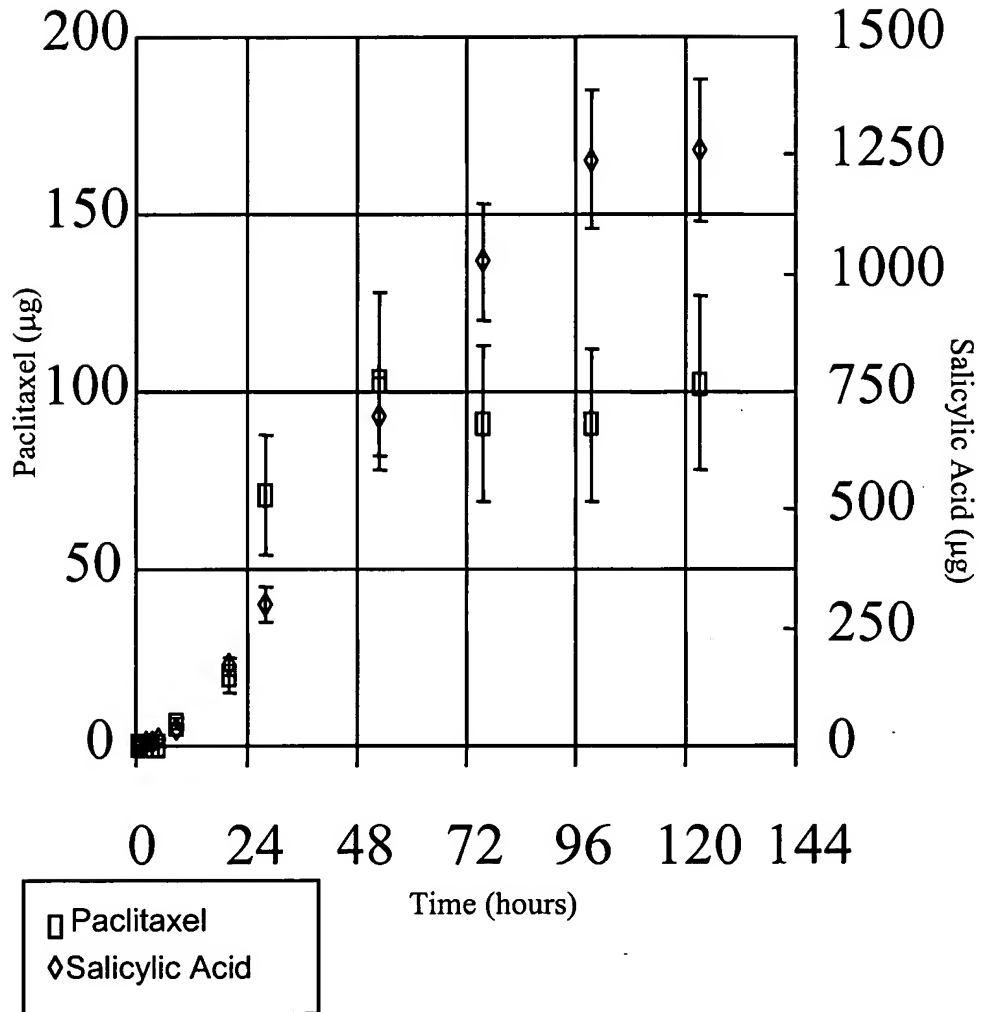


**Figure 8B**





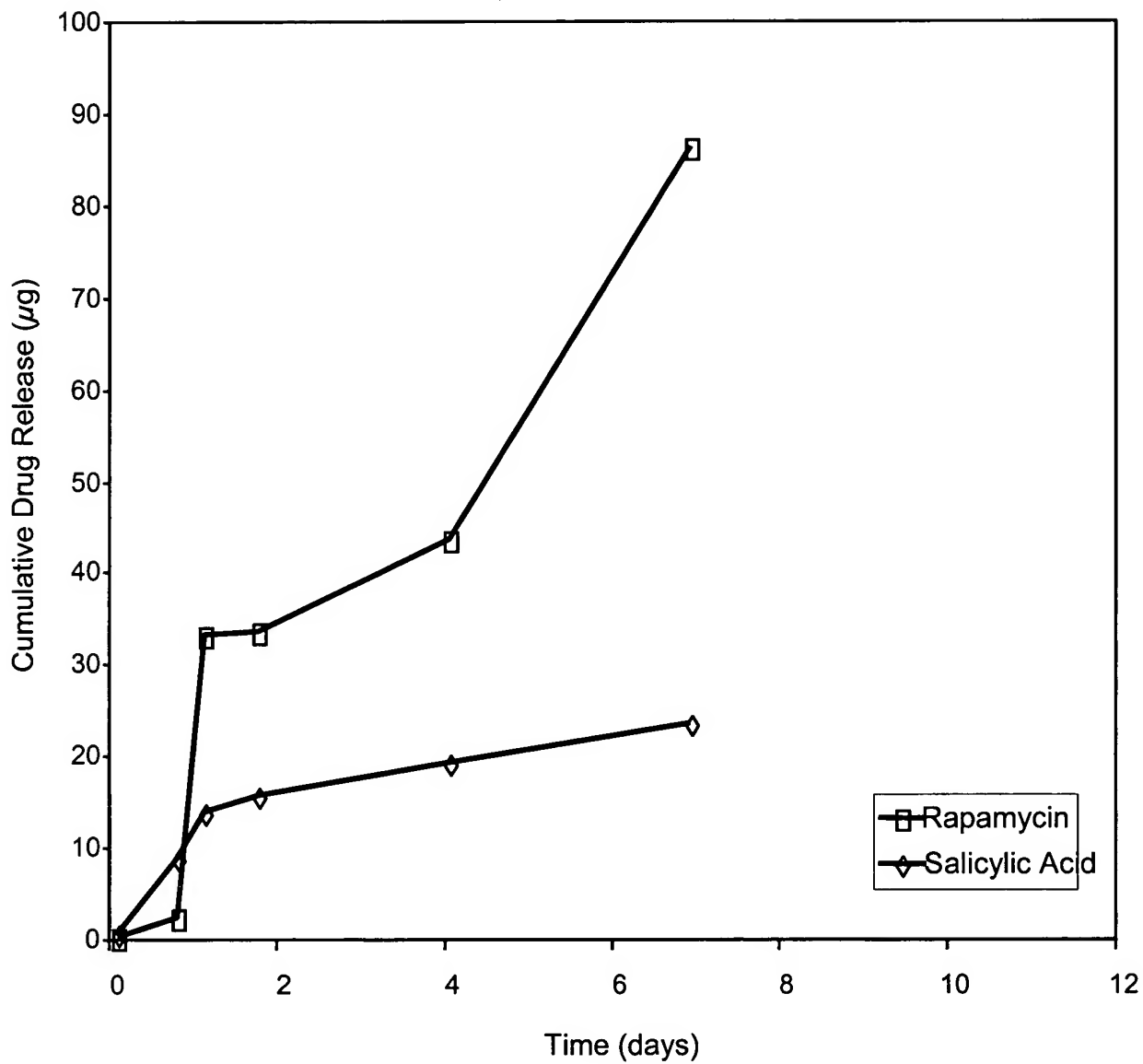
**Figure 9A**



**Figure 9B**

Property	Formulation			
	PX510	PX721	PX261	PX749
T <sub>g</sub> (°C)	44	38	29	16
Tensile modulus (MPa)	2.0 (25 °C) 5.1 (37 °C)			3.0 (25 °C)
Yield Strength (MPa)	Not observed			6.0 (25 °C)
Ultimate Elongation (%)	1.5 (25 °C) 350 (37 °C)			500 (25 °C)

**Figure 10**



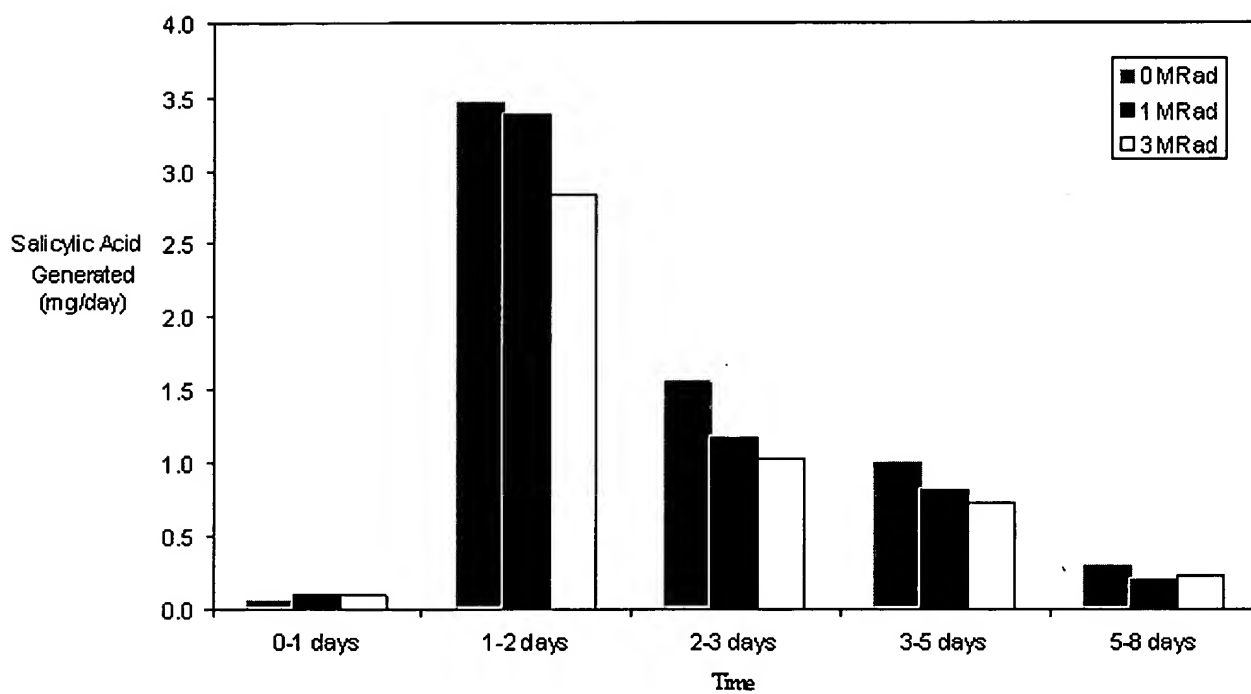
**Figure 11**

Attorney Docket No. 04271500  
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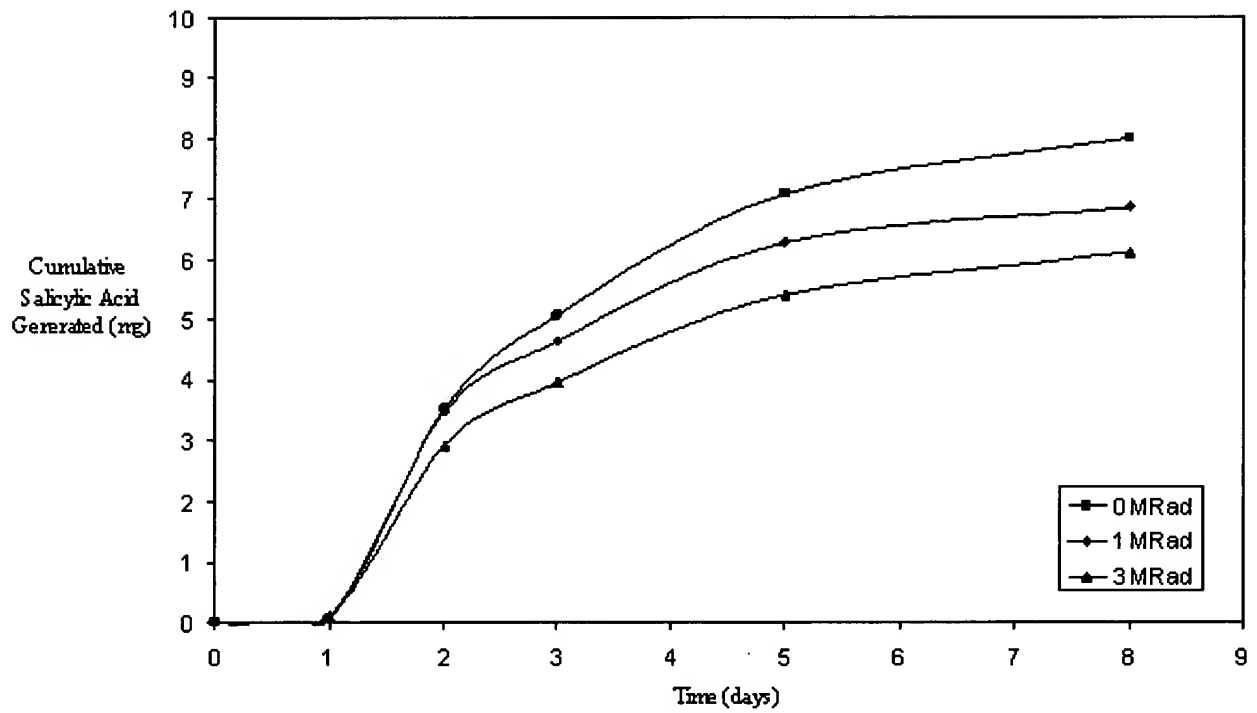
Property	E Beam (3 MRad)			$\gamma$ (25-35 KGys)		
	PX510	PX721	PX261	PX510	PX721	PX261
MW	-26%	-39%	-26%	-14%	N/C	N/C
Hardness	-2 units	N/C	-1 unit	N/C	-3 units	-2 units
Flexibility	N/C	N/C	N/C	N/C	N/C	N/C
Adhesion	N/C	N/C	-1 unit	N/C	N/C	N/C

N/C: no change

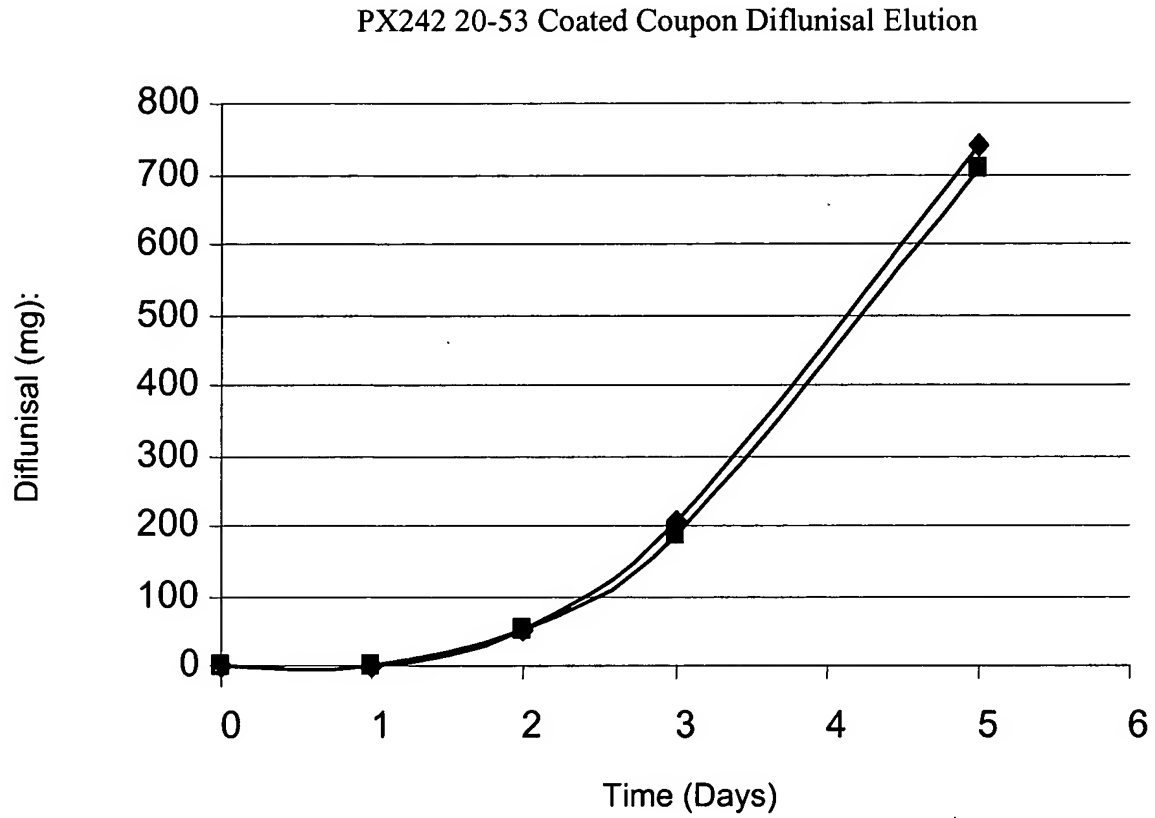
**Figure 12**



**Figure 13A**

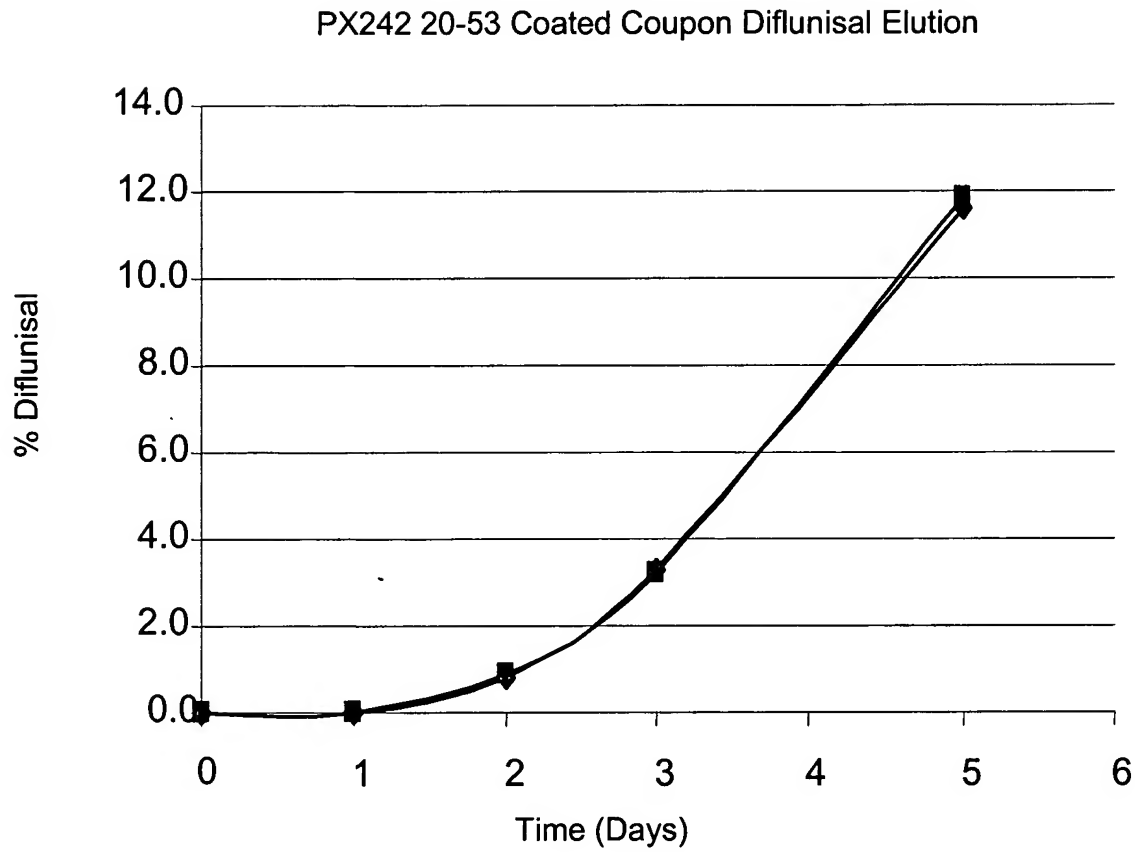


**Figure 13B**



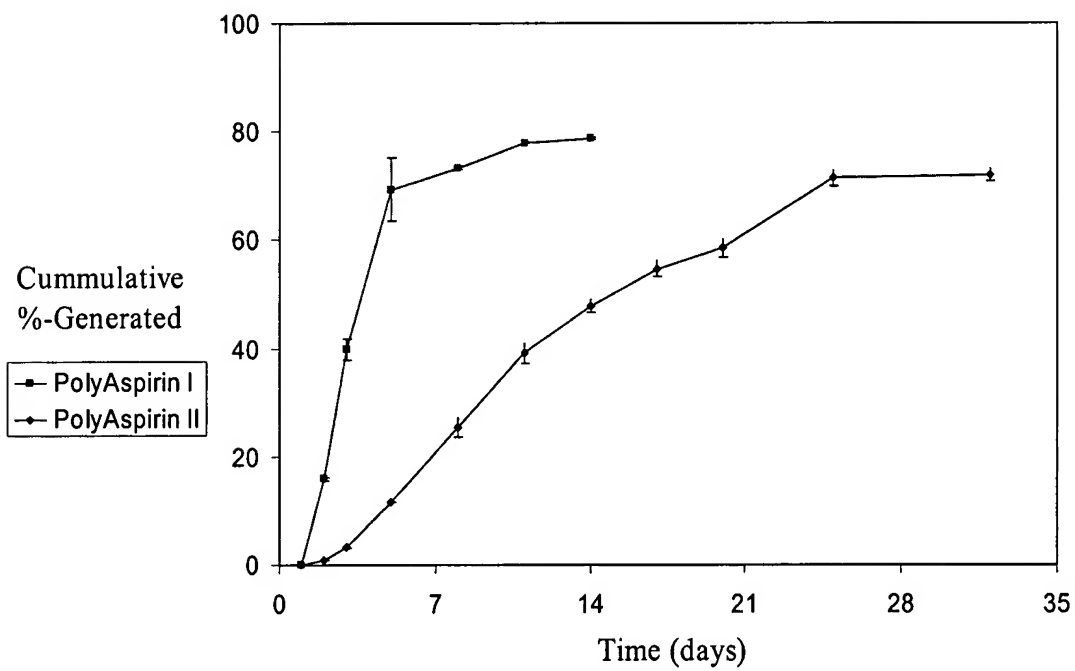
**Figure 14**





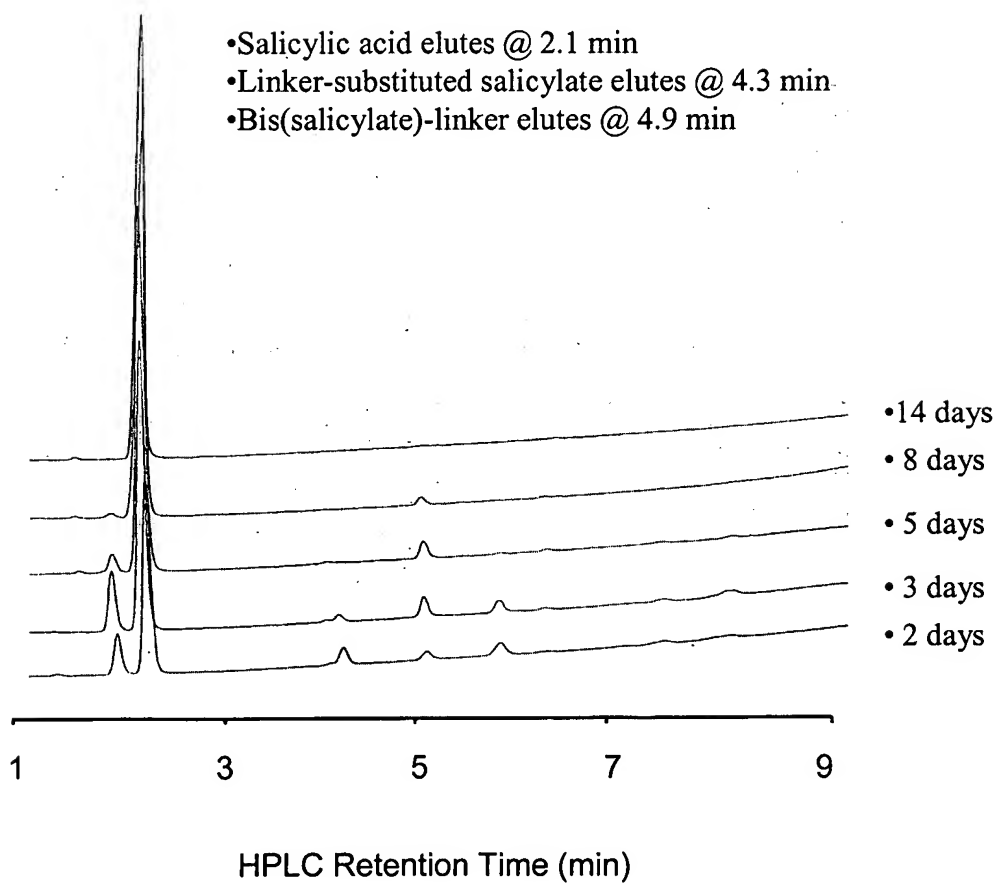
**Figure 15**

Erosion of PolyAspirin I & II  
Generation of NSAID into 37 °C pH 7.4 PBS from  
~5  $\mu\text{m}$ -thick Coatings on 316L SS Plates



**Figure 16**

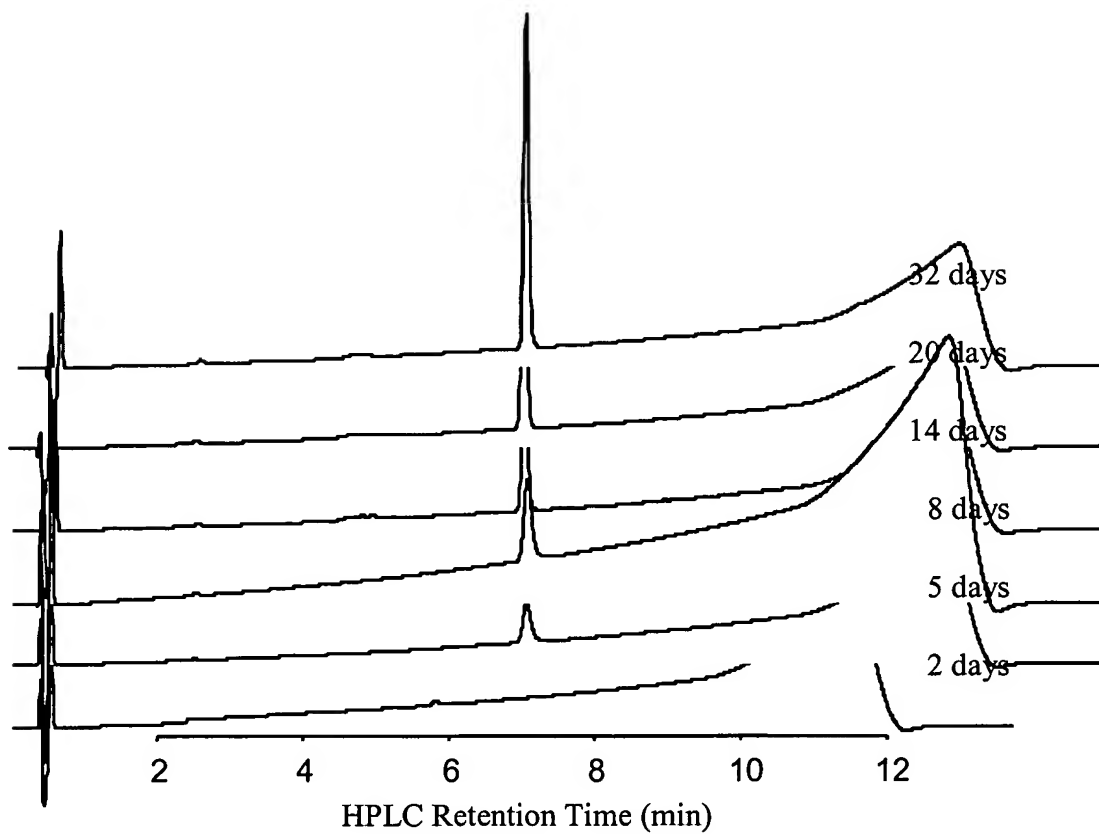
Erosion Profile for PolyAspirin I



**Figure 17**

Erosion Profile for PolyAspirin II

DiFlunisal elutes @ 7.1 min  
Linker-substituted DiFlunisal elutes @ 9.0 min  
Bis(diFlunisal)-linker elutes @ 12 min



**Figure 18**

Effect of MW on Erosion

Generation of Diflunisal from PolyAspirin II into  
37 °C Serum from Coatings on 316L SS Plates

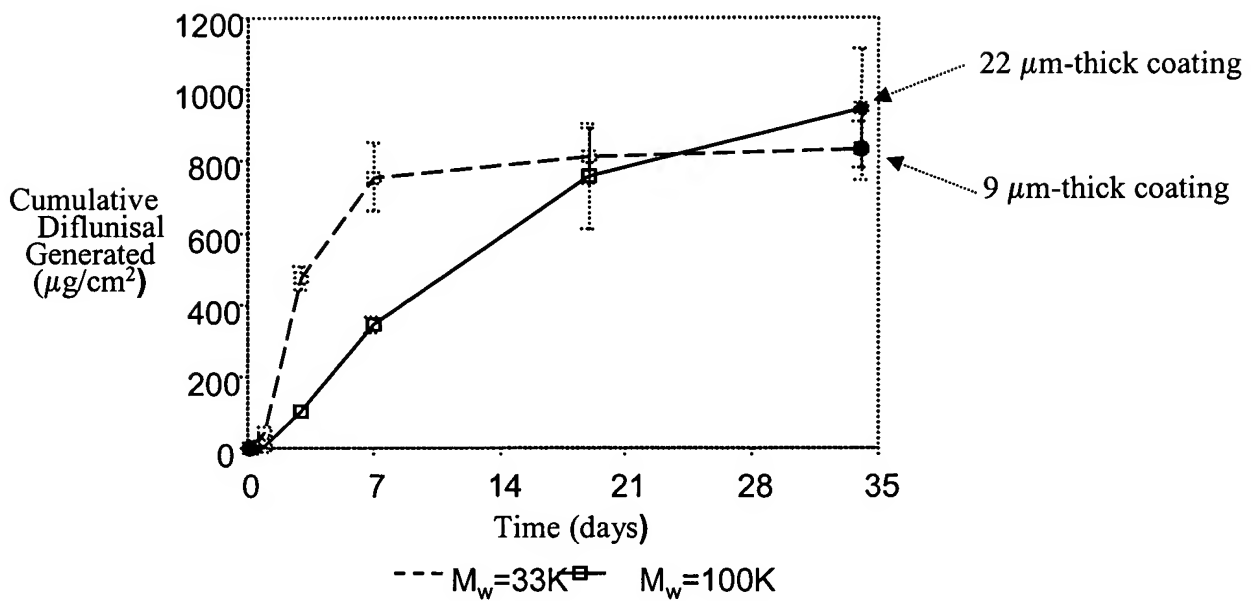


Figure 19

Tuning Mechanical Properties

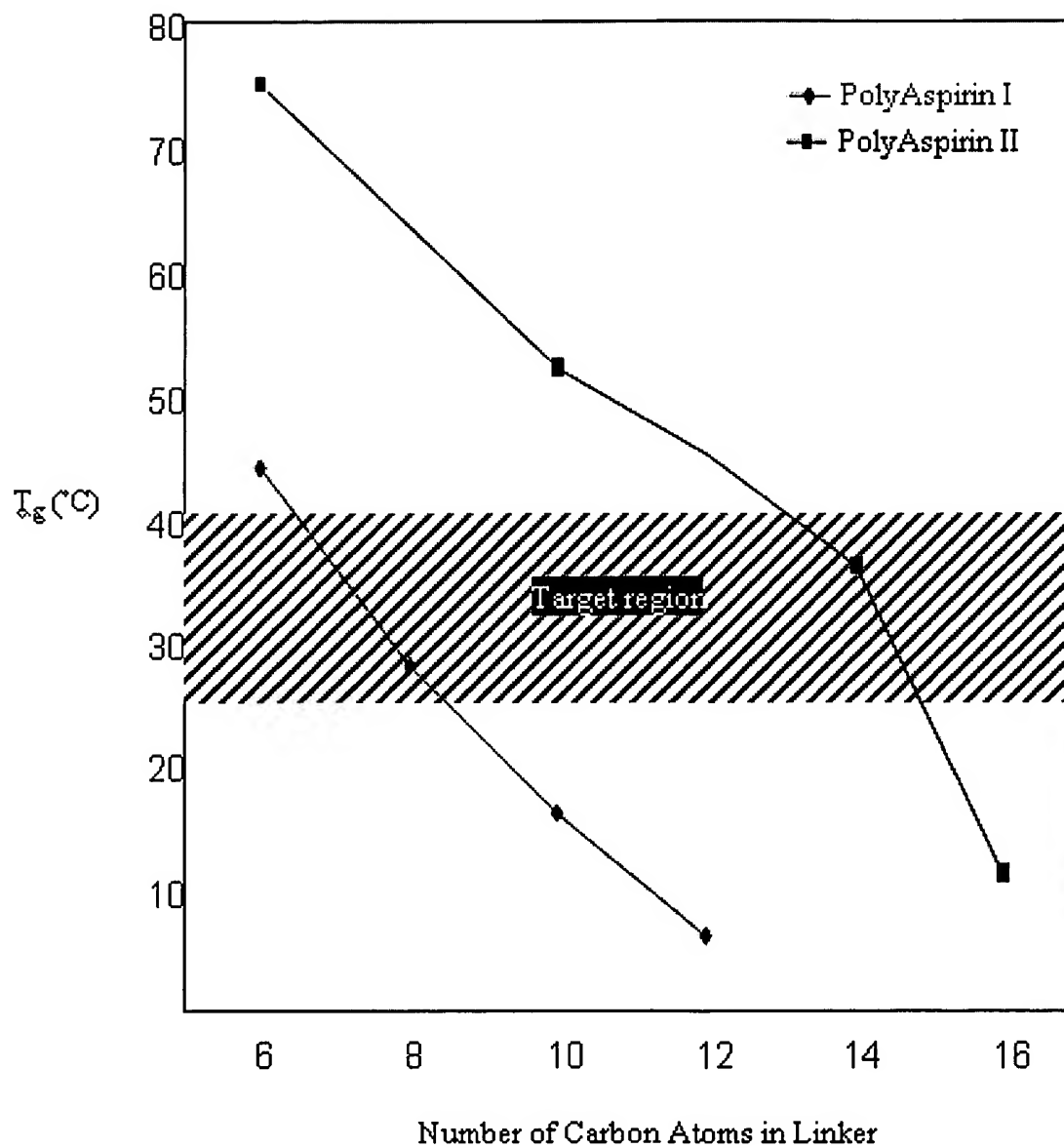


Figure 20

Thermoanalysis of PolyAspirin™

Property	PolyAspirin I	PolyAspirin II	
	PX261 M <sub>w</sub> ~ 20K	PX657 M <sub>w</sub> ~ 33K	M <sub>w</sub> ~ 100K
T <sub>g</sub> (°C)	29	36	44
Ultimate Stress (kPa)	1700 (25°C) >2000 (37°C)	>2800 (25°C)	>2600 (25°C)
Ultimate Elongation (%)	>500 (25°C) >500 (37°C)	>4 (25°C)	>500 (25°C)
Toughness (kPa)	>3900 (25°C) >4400 (37°C)	>560 (25°C)	>4000 (25°C)

Figure 21

Properties of PolyAspirin™ Coatings

Test	PolyAspirin I	PolyAspirin II	
	PX261 Mw ~ 20K	PX657 Mw ~ 33K	Mw ~ 100K
<u>Hardness</u>			
Ambient	B	F	3H
5 min in PBS, 37 °C	B	2B	B
1 hr in PBS, 37 °C	-	8B	4B
<u>Flexibility</u>			
Ambient	<3 mm	<3 mm	<3 mm
5 min in PBS, 37 °C	<3 mm	<3 mm	<3 mm
1 hr in PBS, 37 °C	-	<3 mm	<3 mm
<u>Adhesion</u>			
Ambient	5B	5B	5B

Figure 22



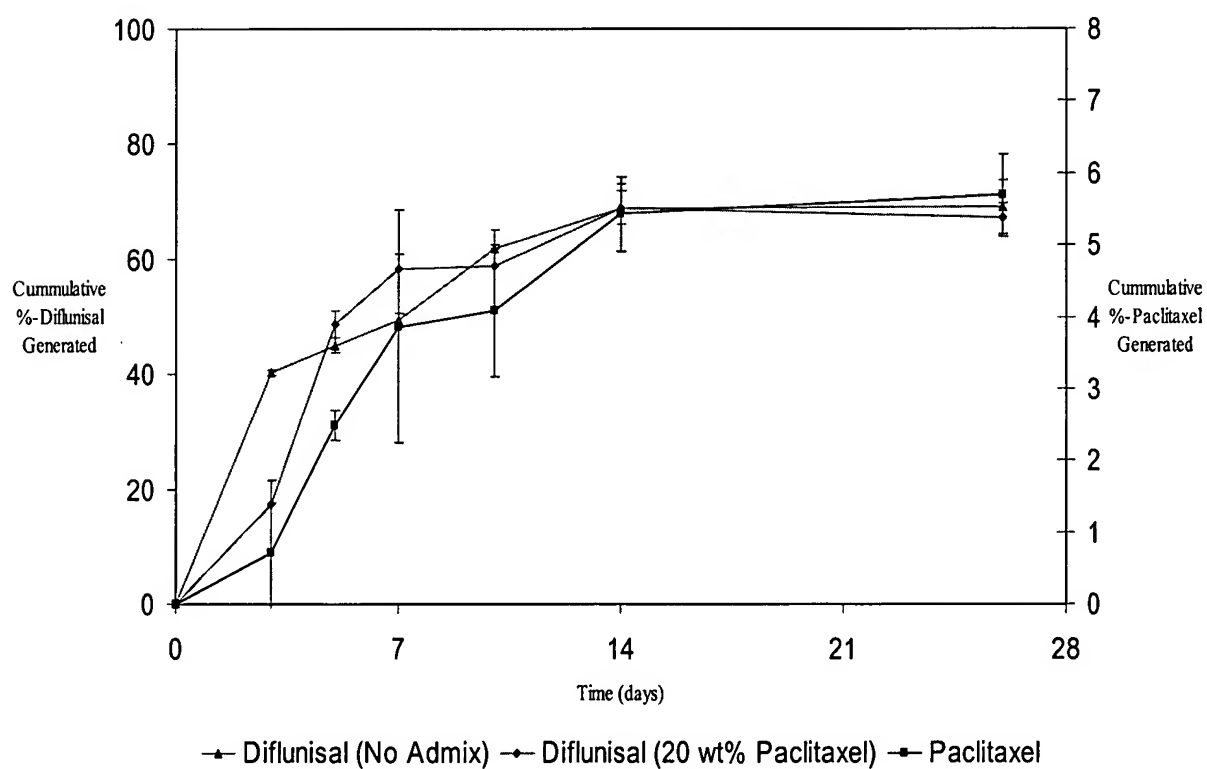
PolyAspirin Coatings with Admixtures

Test	PolyAspirin II (PX657)	
	No Admixture	20% Paclitaxel Admixed
<u>Hardness</u>		
Ambient	F	F
5 min in PBS, 37 °C	2B	F
1 hr in PBS, 37 °C	8B	6B
<u>Flexibility</u>		
Ambient	<3 mm	<3 mm
5 min in PBS, 37 °C	<3 mm	<3 mm
1 hr in PBS, 37 °C	<3 mm	<3 mm
<u>Adhesion</u>		
Ambient	5B	5B

**Figure 23**

### Erosion of PolyAspirin I & II

Diffunisal Generation & Paclitaxel Release into 37 °C Serum from ~5  $\mu$ m-thick Coatings on 316L SS Plates



**Figure 24**

Erosion of Sterilized PolyAspirin II

Generation of Diflunisal into 37 °C Serum from ~5  $\mu$ m-thick Coatings on 316L SS Plates

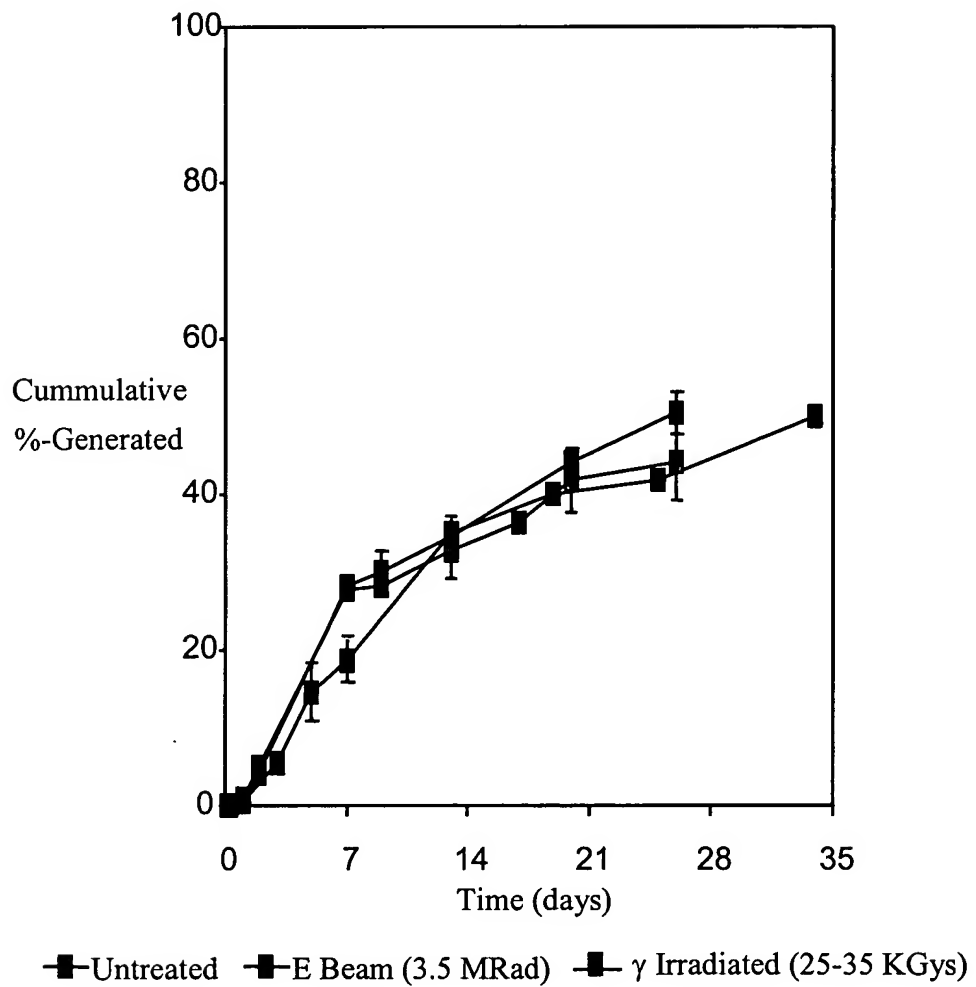


Figure 25

$\gamma$ Irradiation (25-35 Kgys)		
N/C: no change	PolyAspirin I	PolyAspirin II
	PX261 $M_w \sim 20K$	PX657 $M_w \sim 100K$
Property		
MW	N/C	-50%
Hardness	-2 units	-3 units
Flexibility	N/C	-
Adhesion	N/C	-

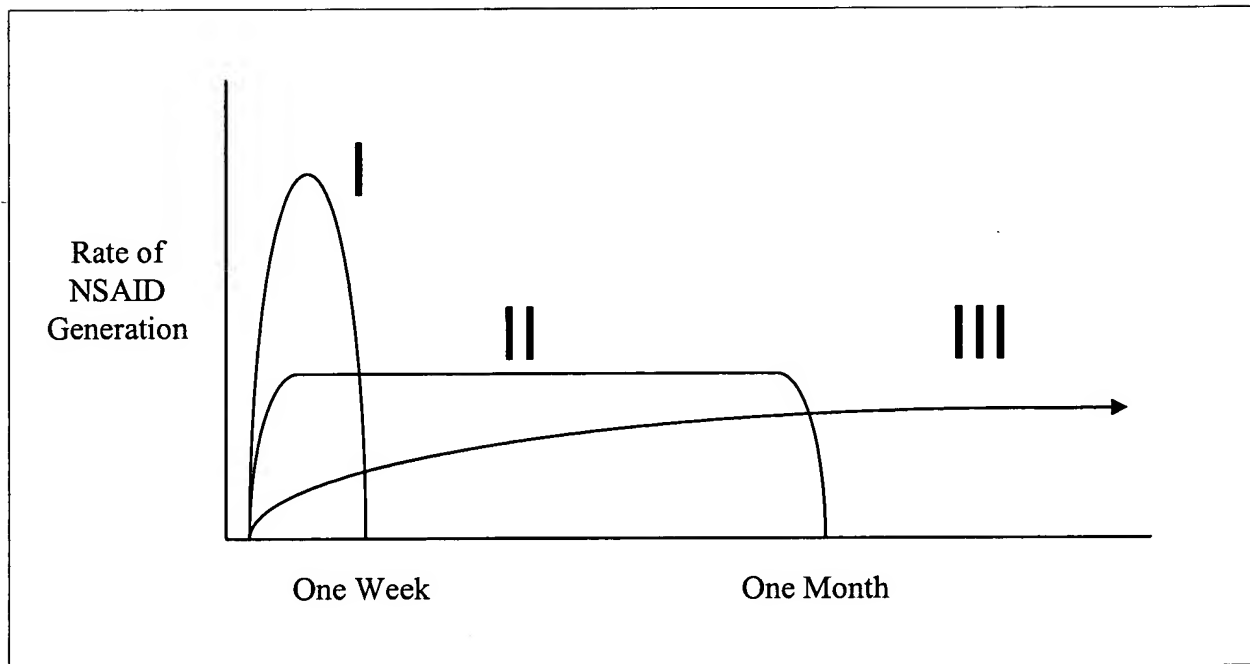
**Figure 26**

E Beam (3-4.5 MRad)

•Property	•PX261 •M <sub>w</sub> ~ 20 K	•M <sub>w</sub> ~ 33K	•M <sub>w</sub> ~ 80K
•MW	•-26%	•+5%	•-30%
•Hardness	•-1 unit •PolyAspirin I	•+2 units •PolyAspirin II	•N/C
•Flexibility	•N/C	•PX657	•N/C
•Adhesion	•-1 unit	•-	•-

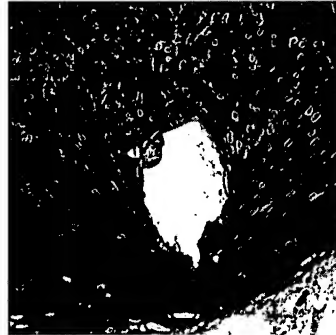
**Figure 27**

**Kinetics of NSAID Generation**



**Figure 28**

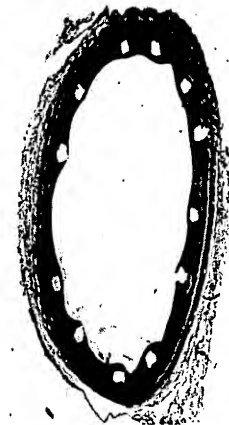
**Figure 29**



**Figure 30**



**Figure 31**



**Figure 32**



**Figure 33**

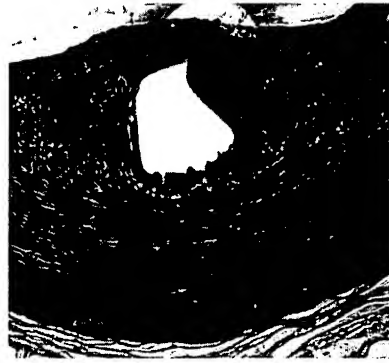
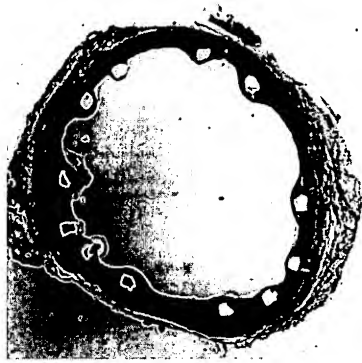


**Figure 34**

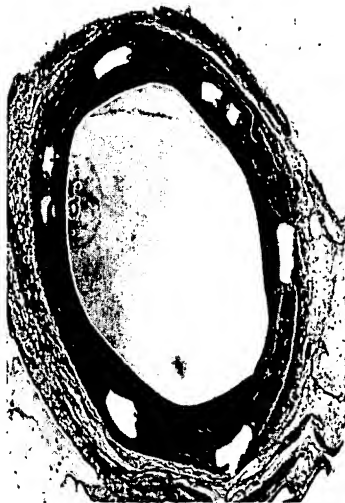




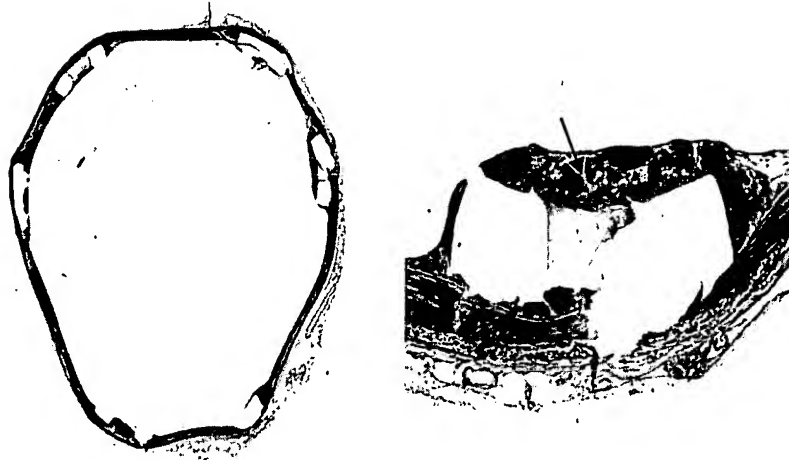
**Figure 35**



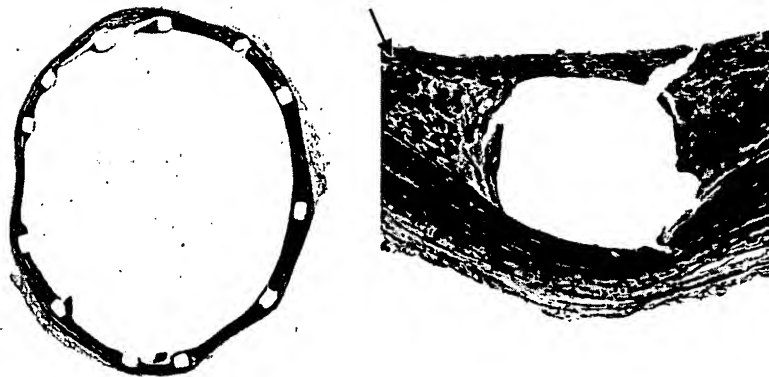
**Figure 36**



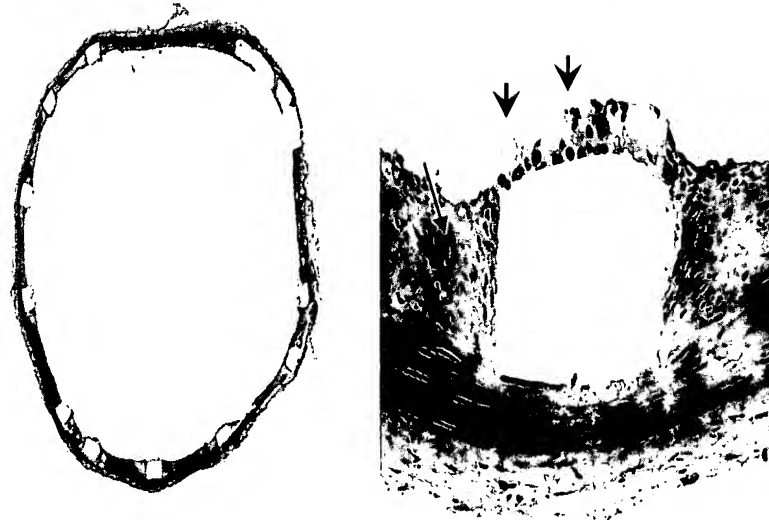
**Figure 37**



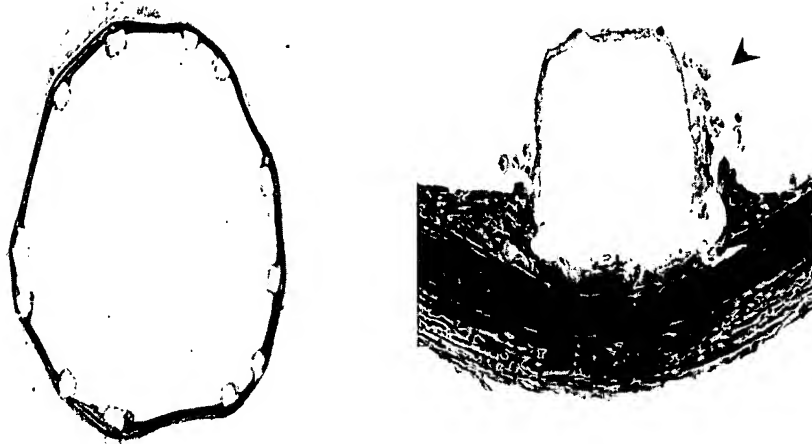
**Figure 38**



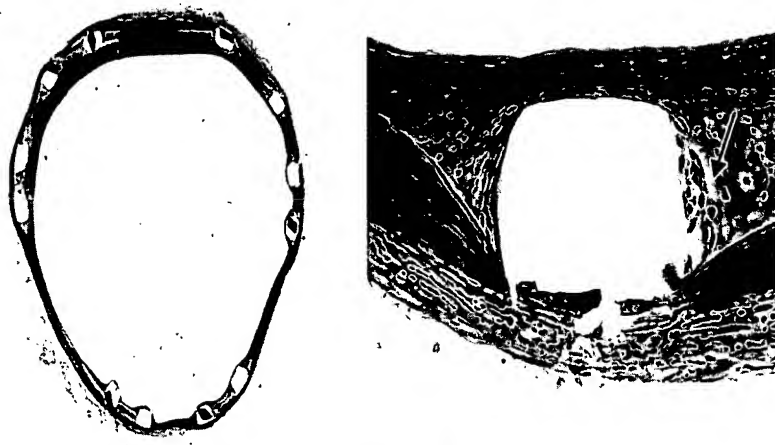
**Figure 39**



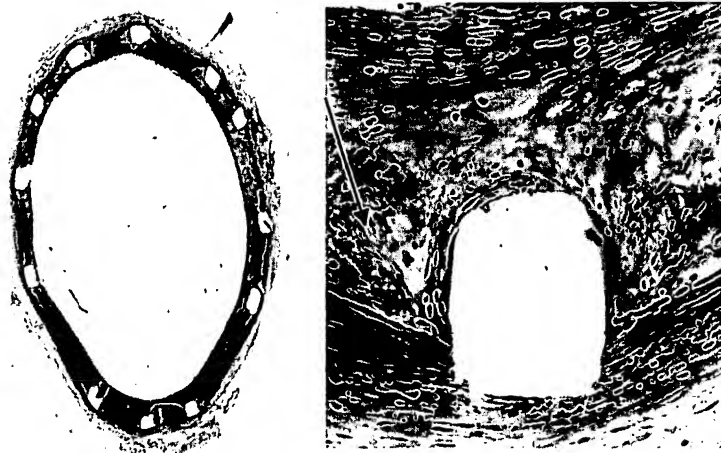
**Figure 40**



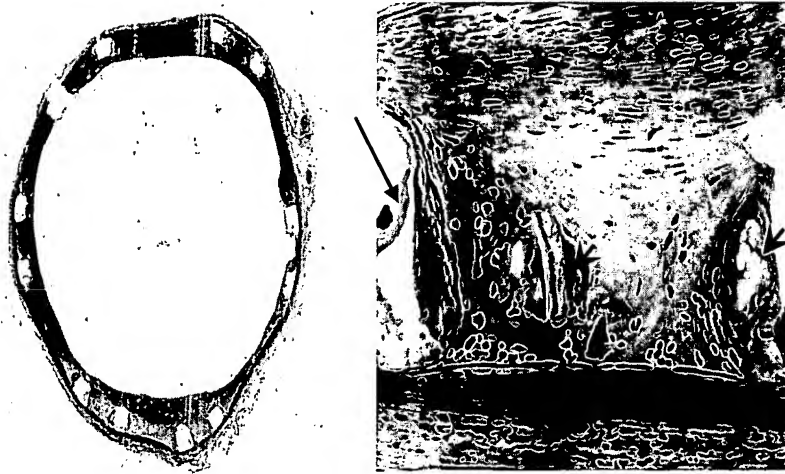
**Figure 41**



**Figure 42**



**Figure 43**



uncrimped/unexpanded

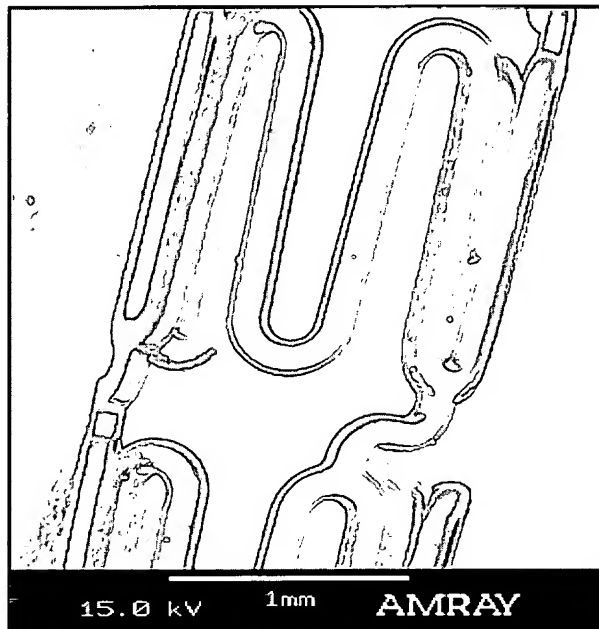


Fig. 44a



Fig. 44b

**Figure 44**

uncrimped/unexpanded

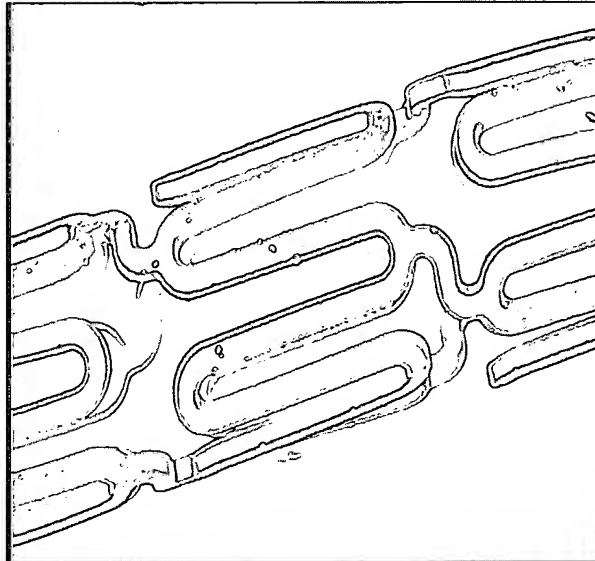


Fig. 45a

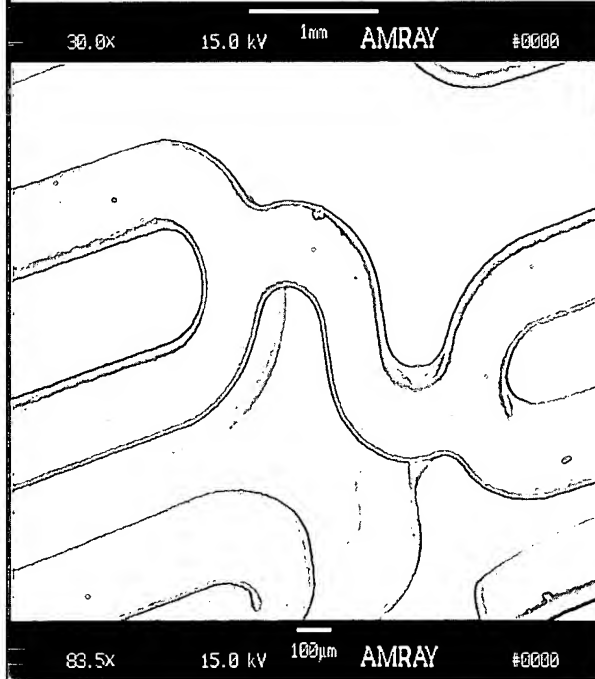


Fig. 45b

**Figure 45**

Uncrimped/unexpanded

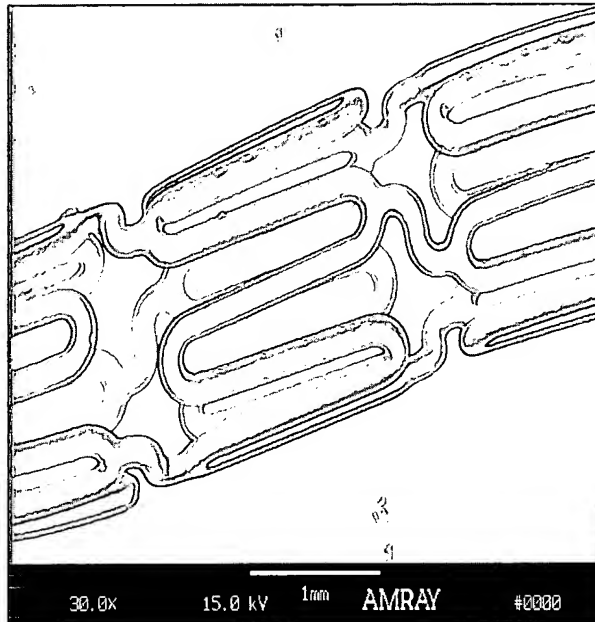


Fig. 46a

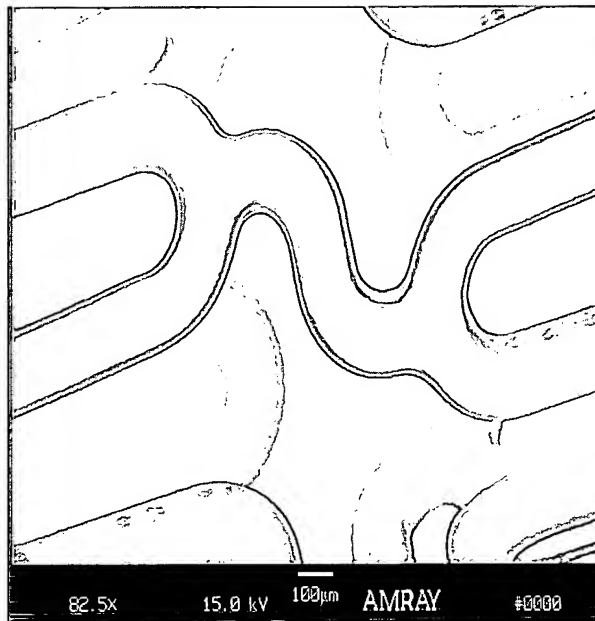
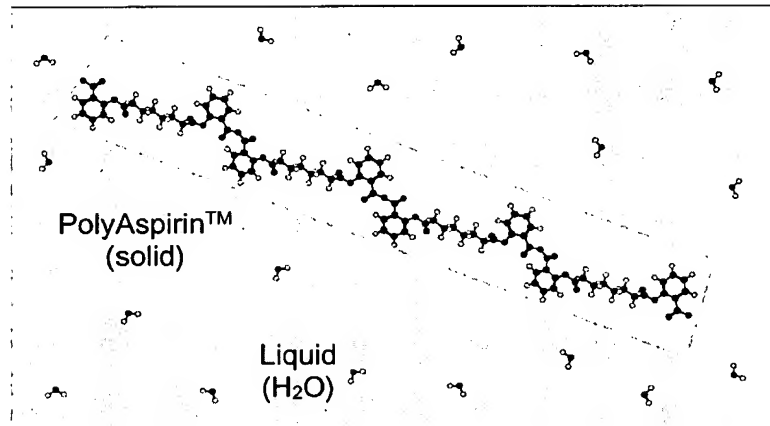


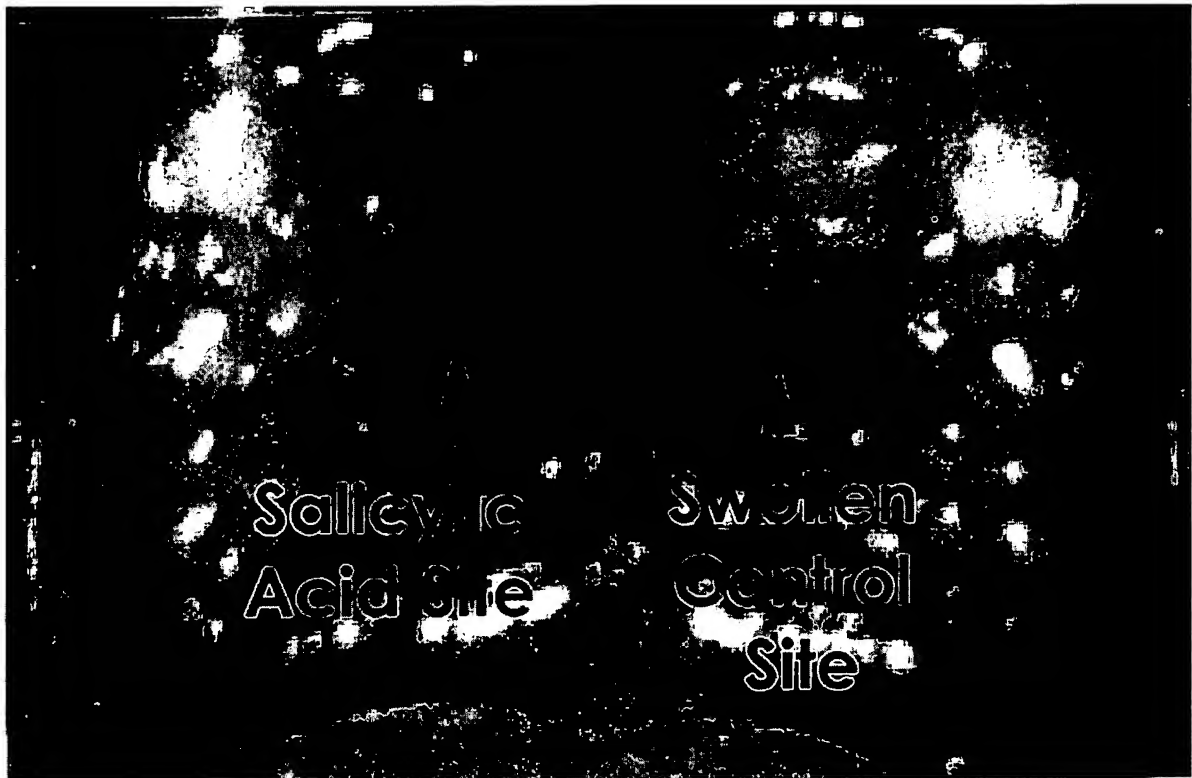
Fig. 46b

Figure 46



**Figure 47**





**Figure 48**

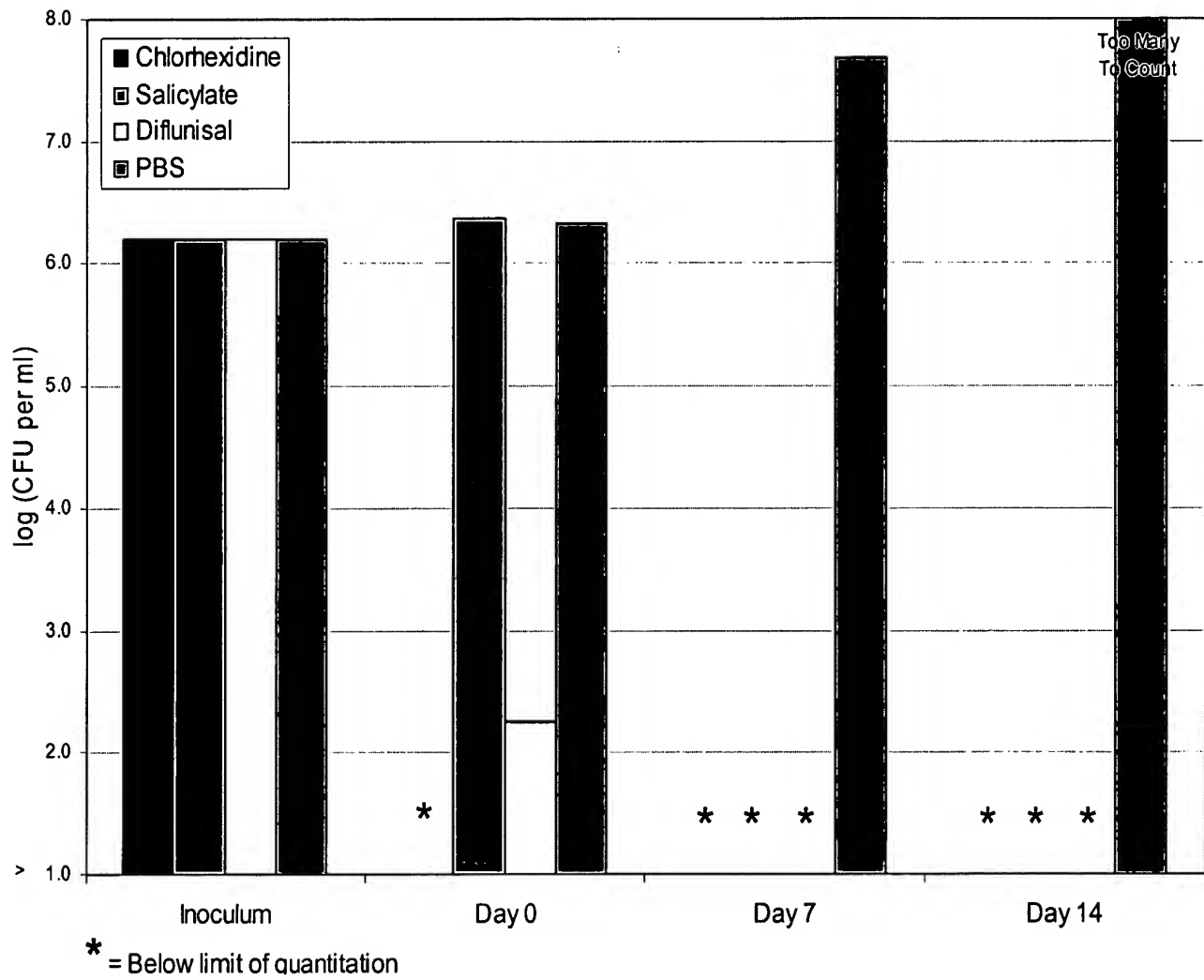
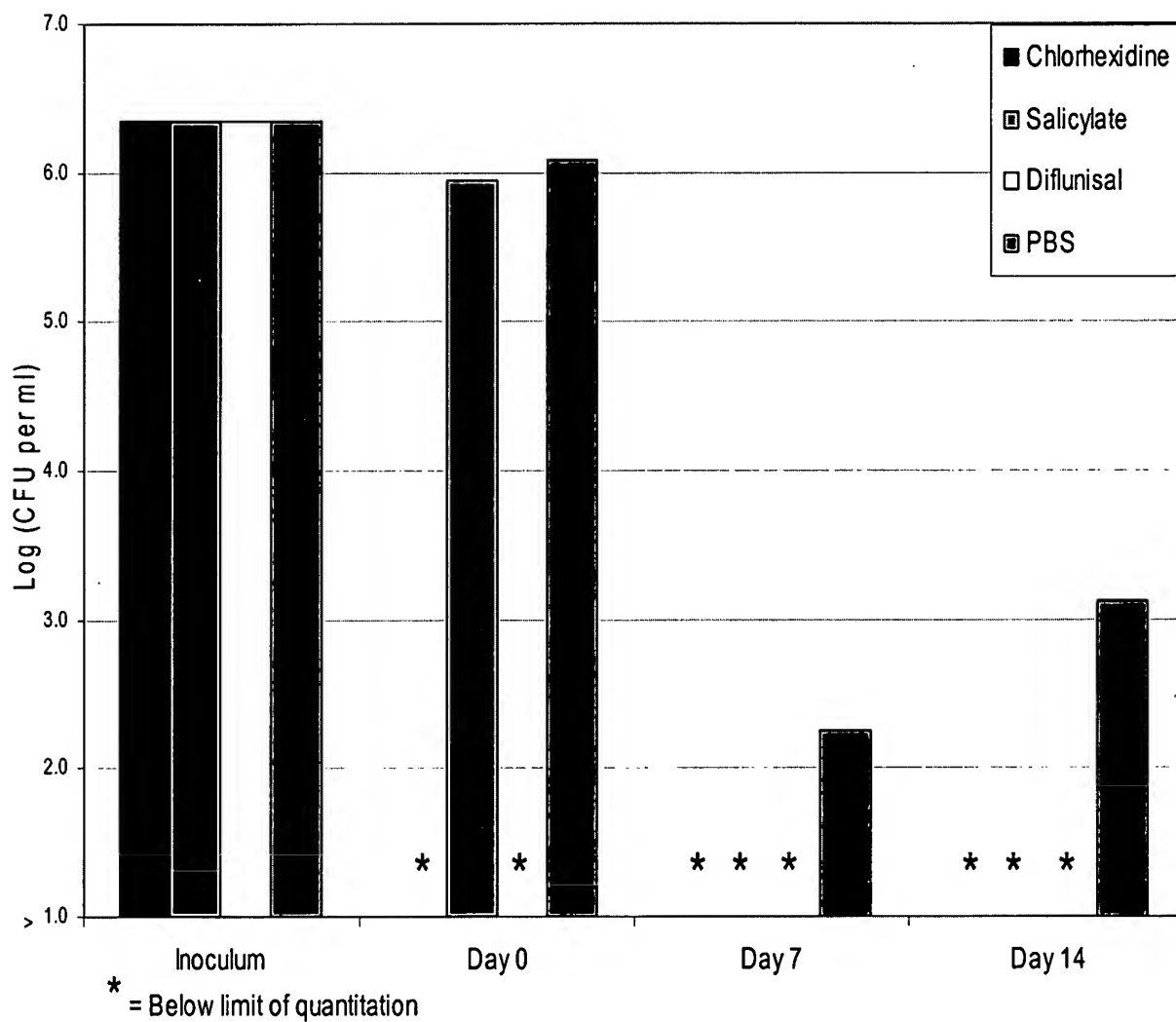
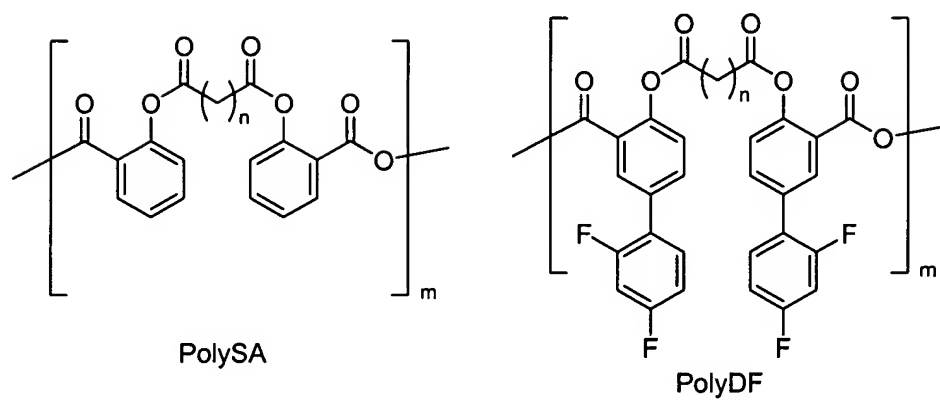


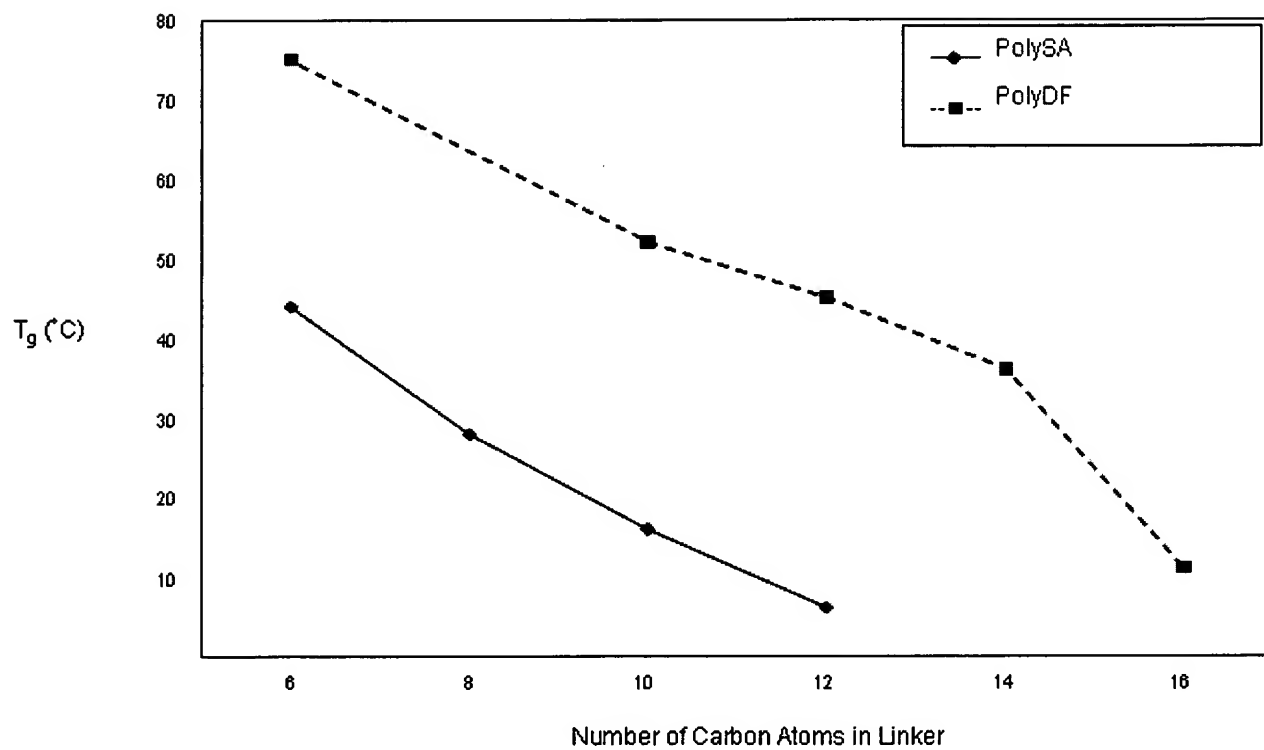
Figure 49



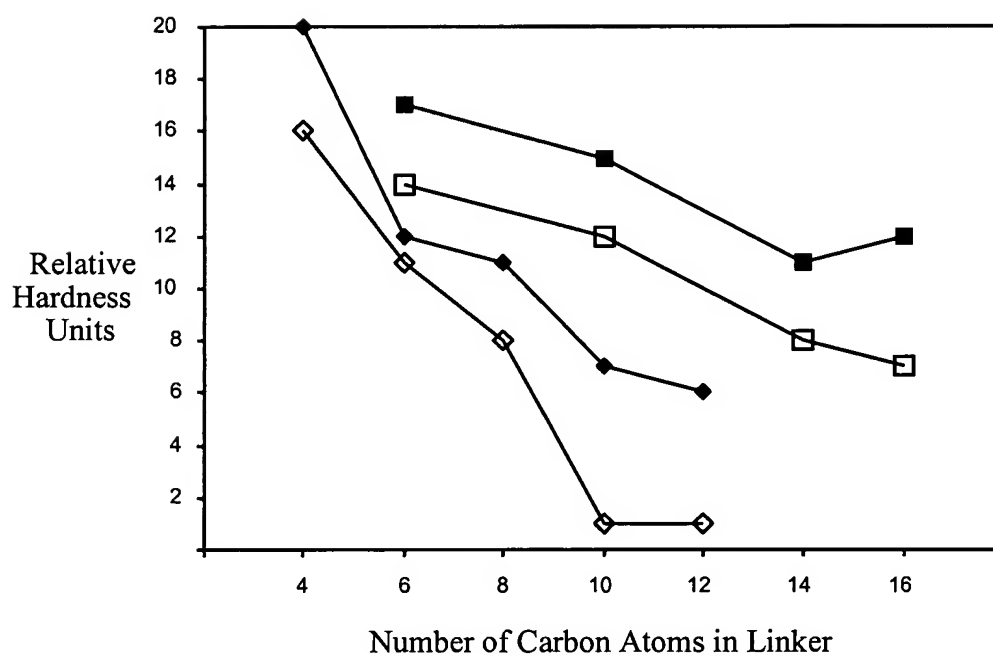
**Figure 50**



**Figure 51**



**Figure 52**



—◆— PolySAA

Closed: Ambient

—■— PolyDF

Open: Soaked 5 min in 37 °C PBS

**Figure 53**

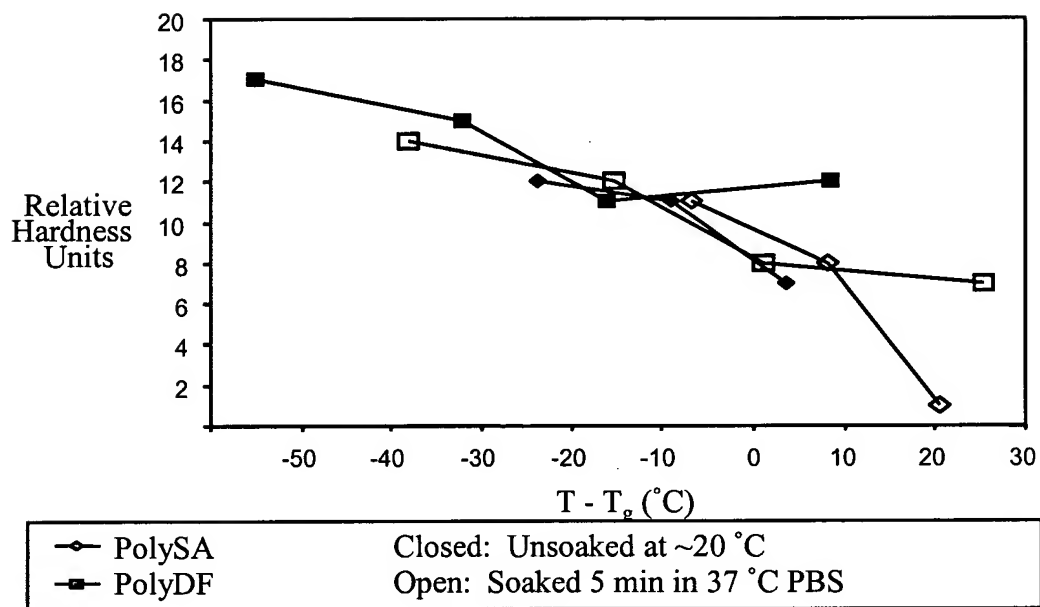


Figure 54

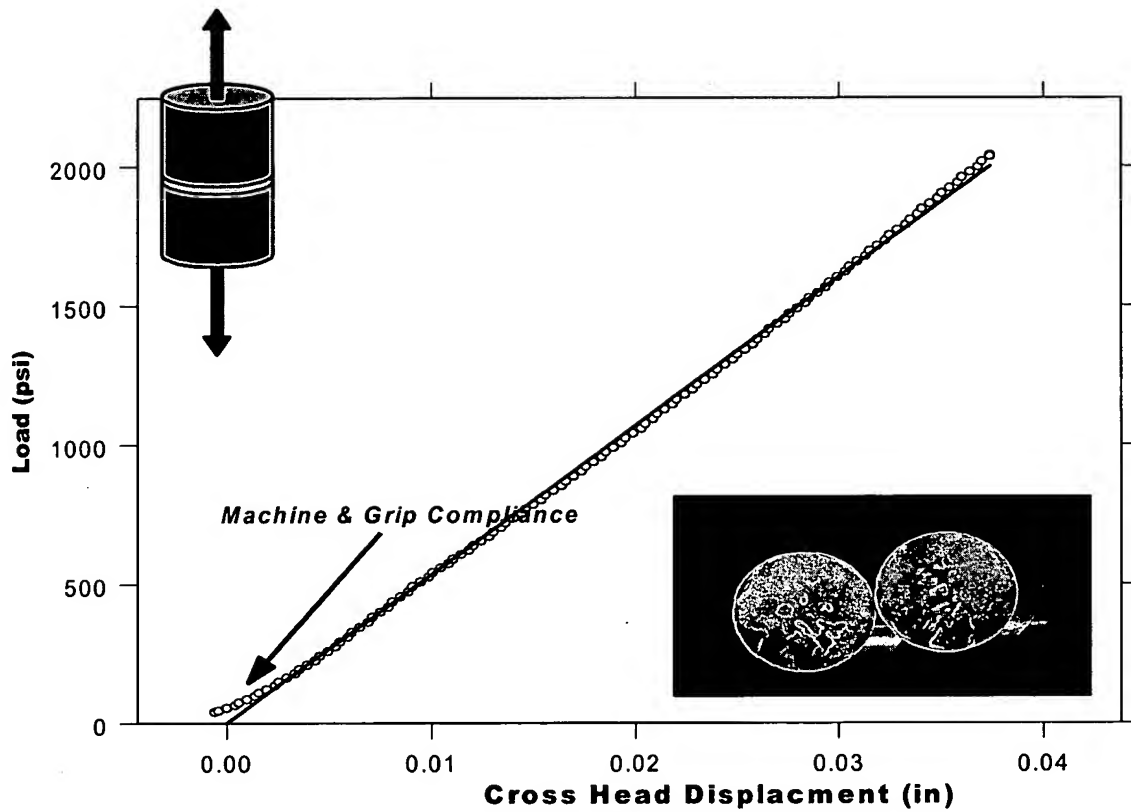


Figure 55



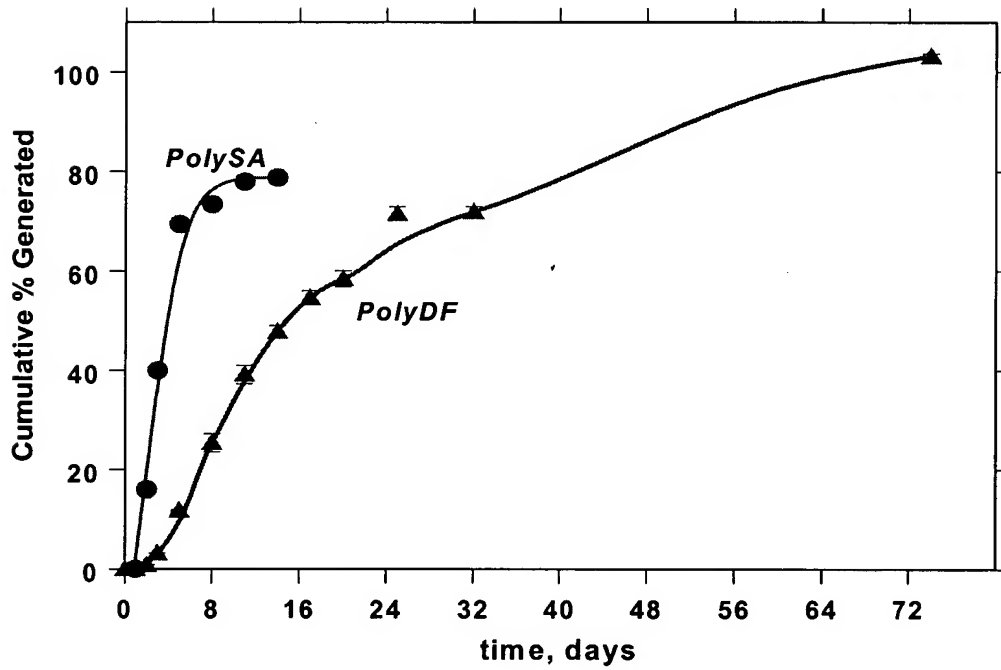
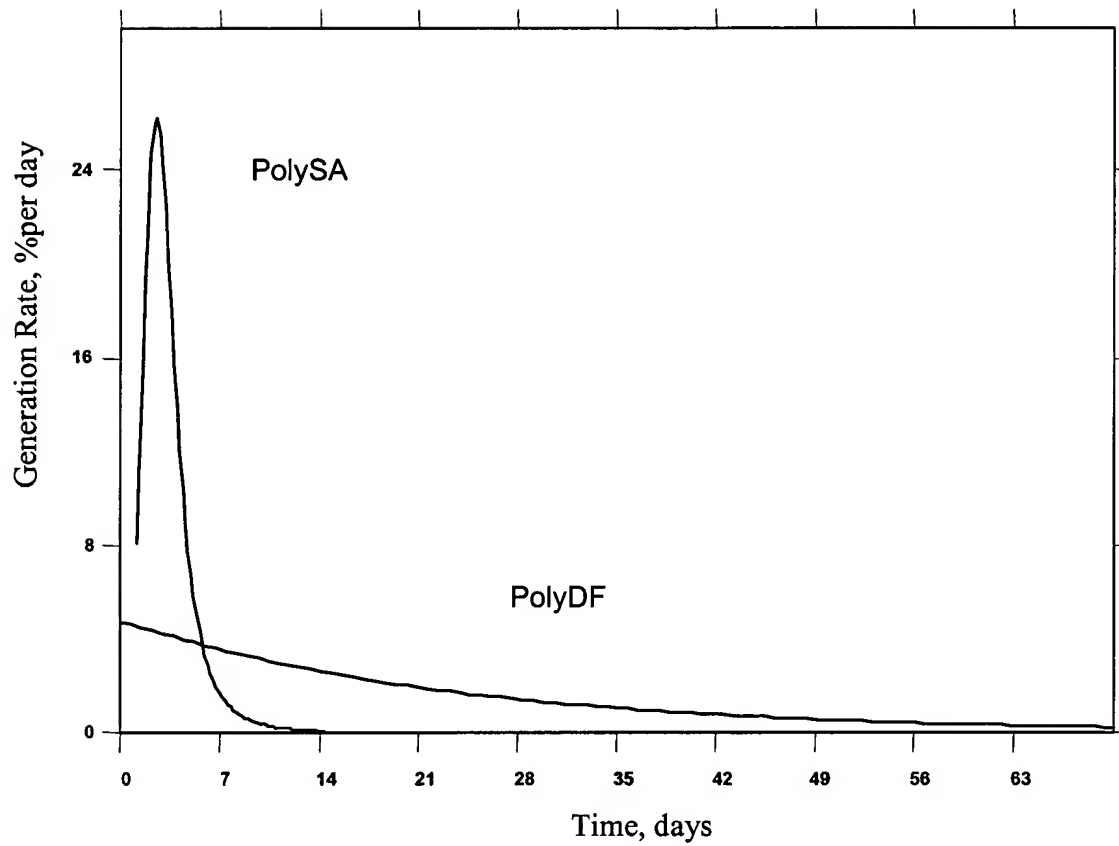


Figure 56



**Figure 57**

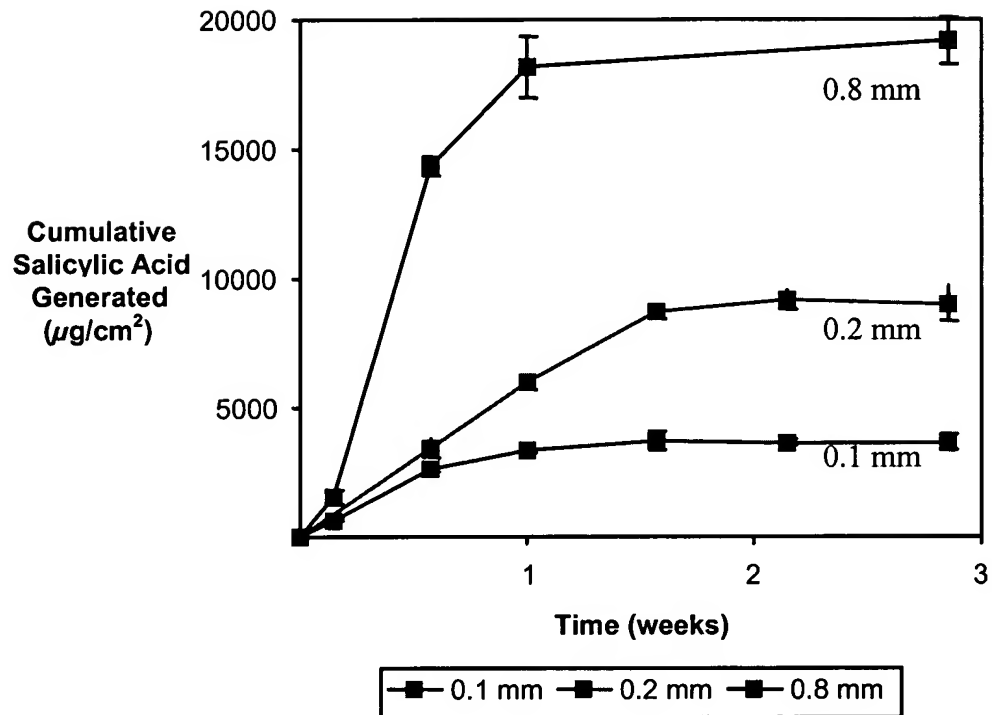


Figure 58

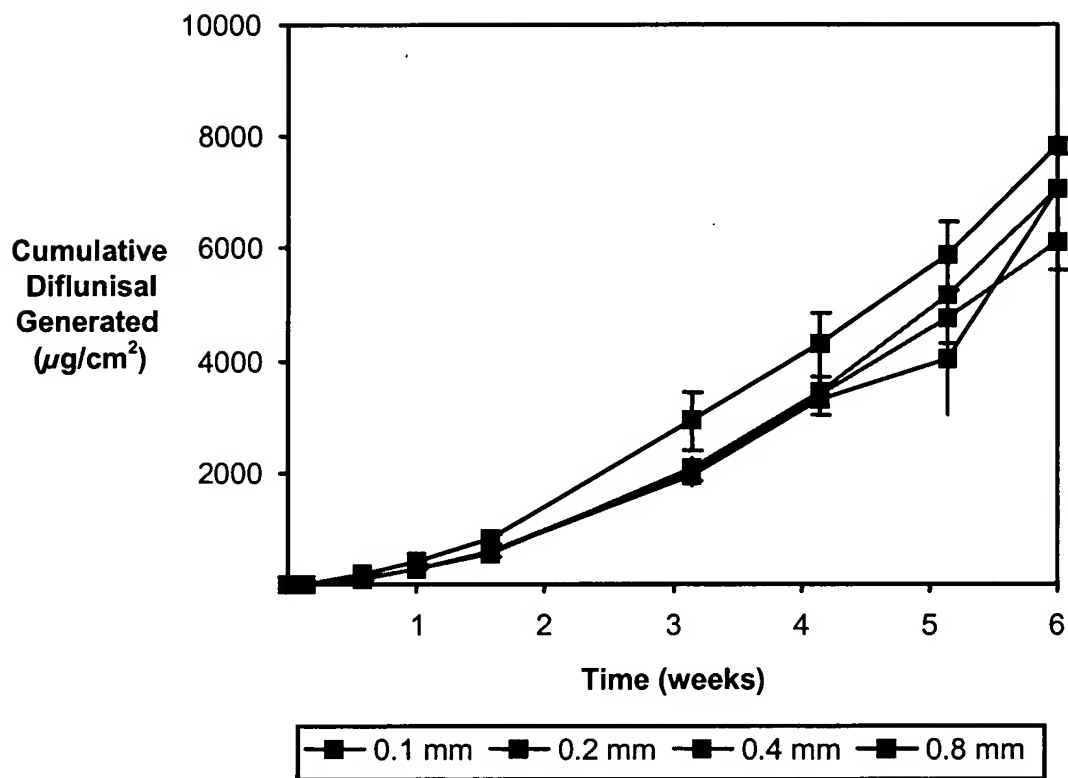
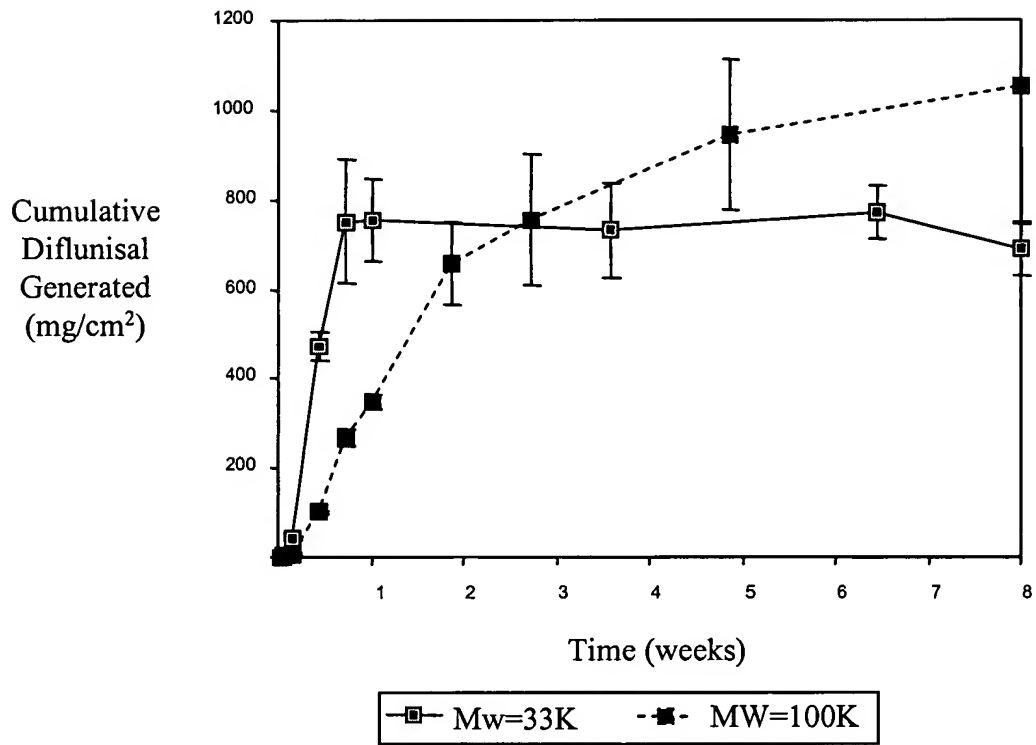


Figure 59



**Figure 60**

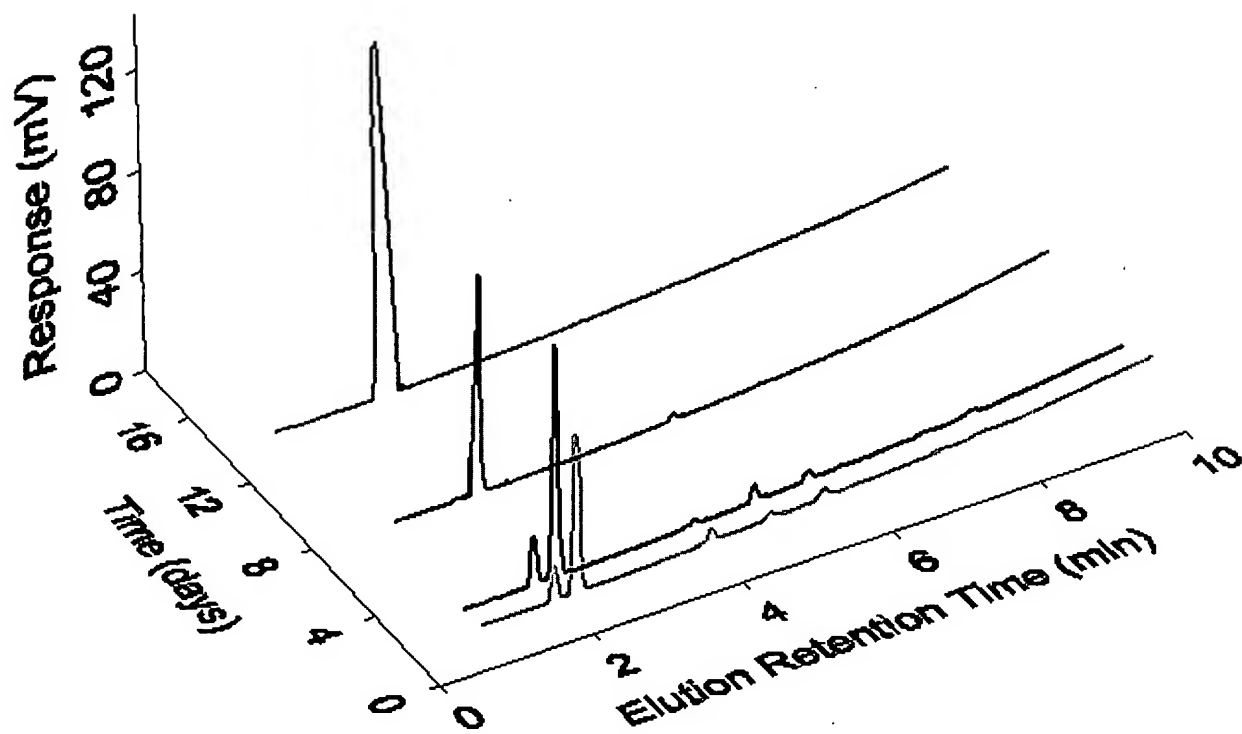
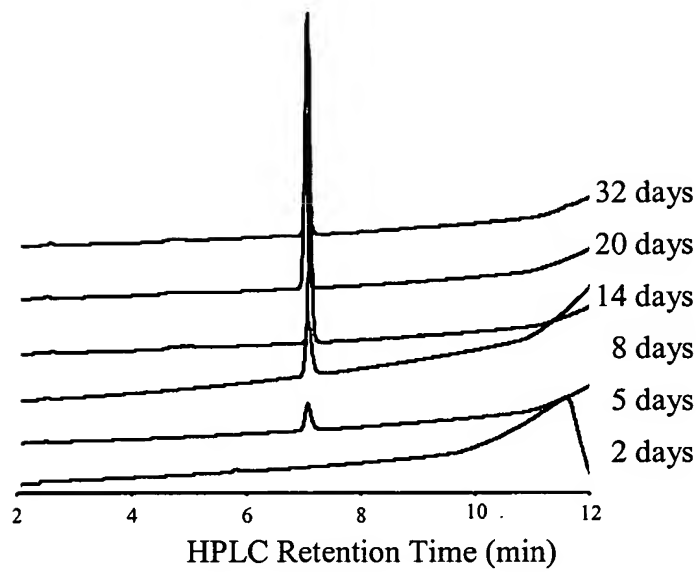


Figure 61



**Figure 62**

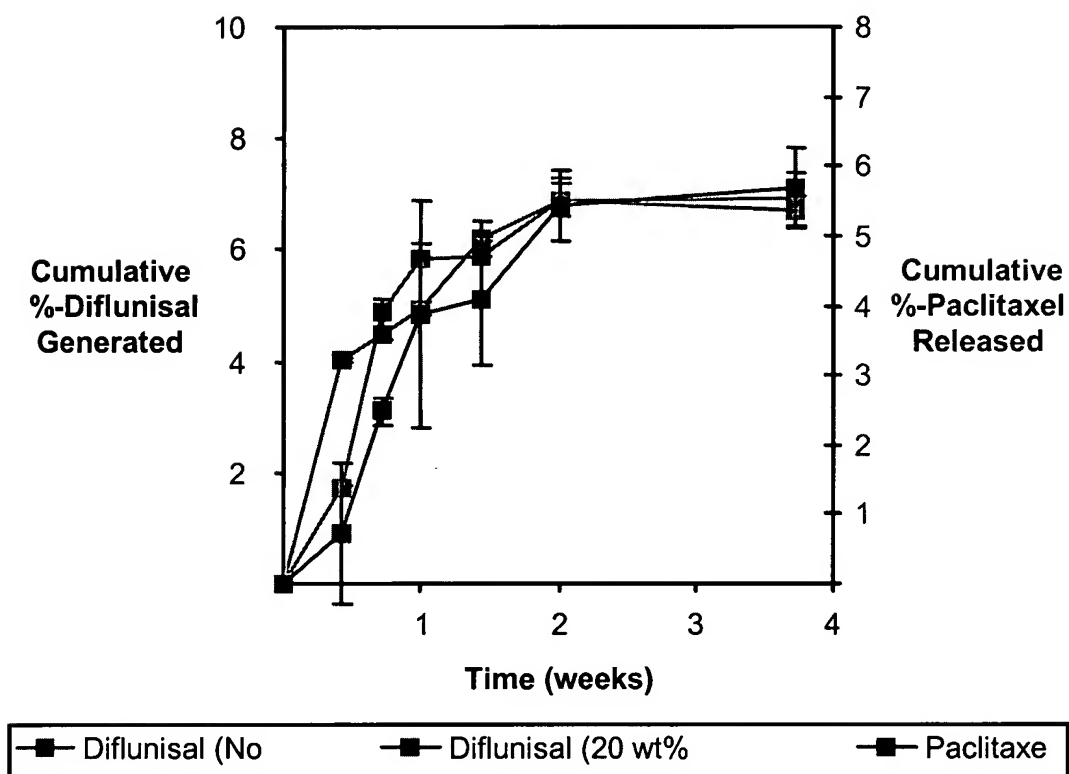


Figure 63



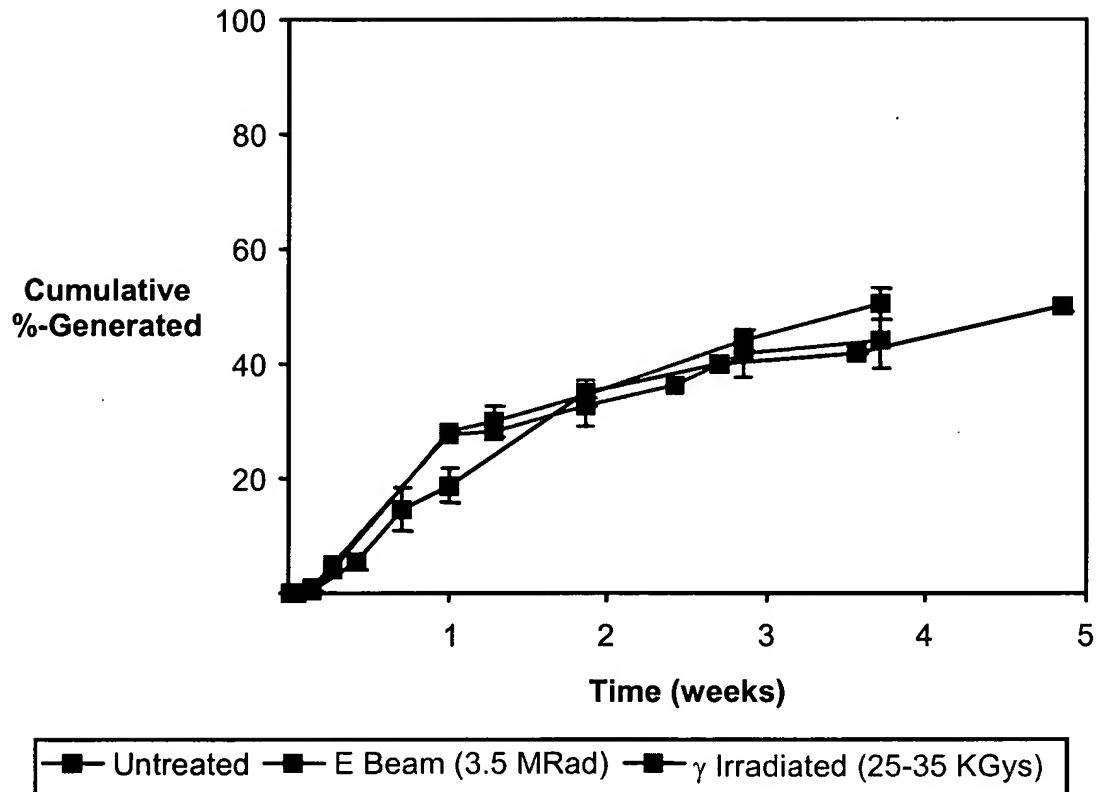


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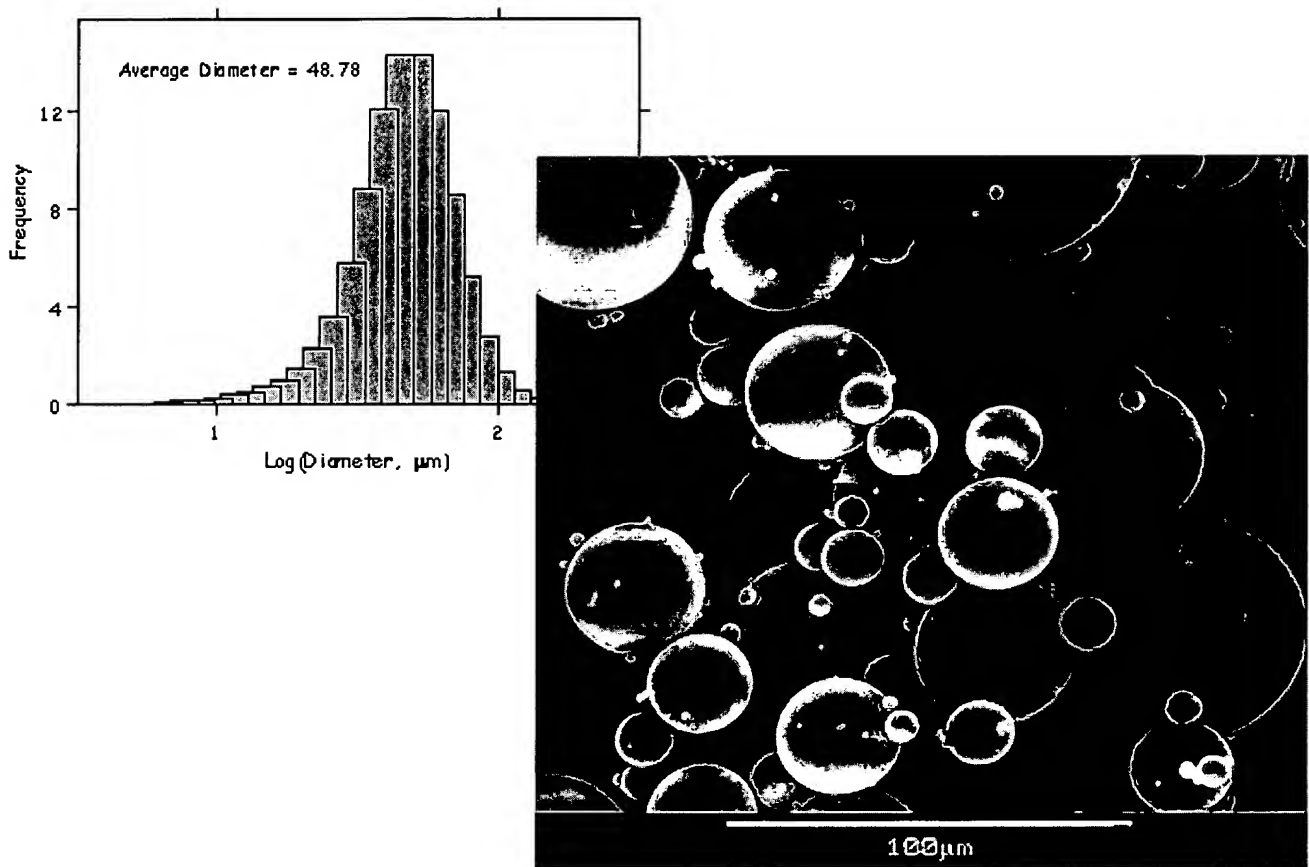
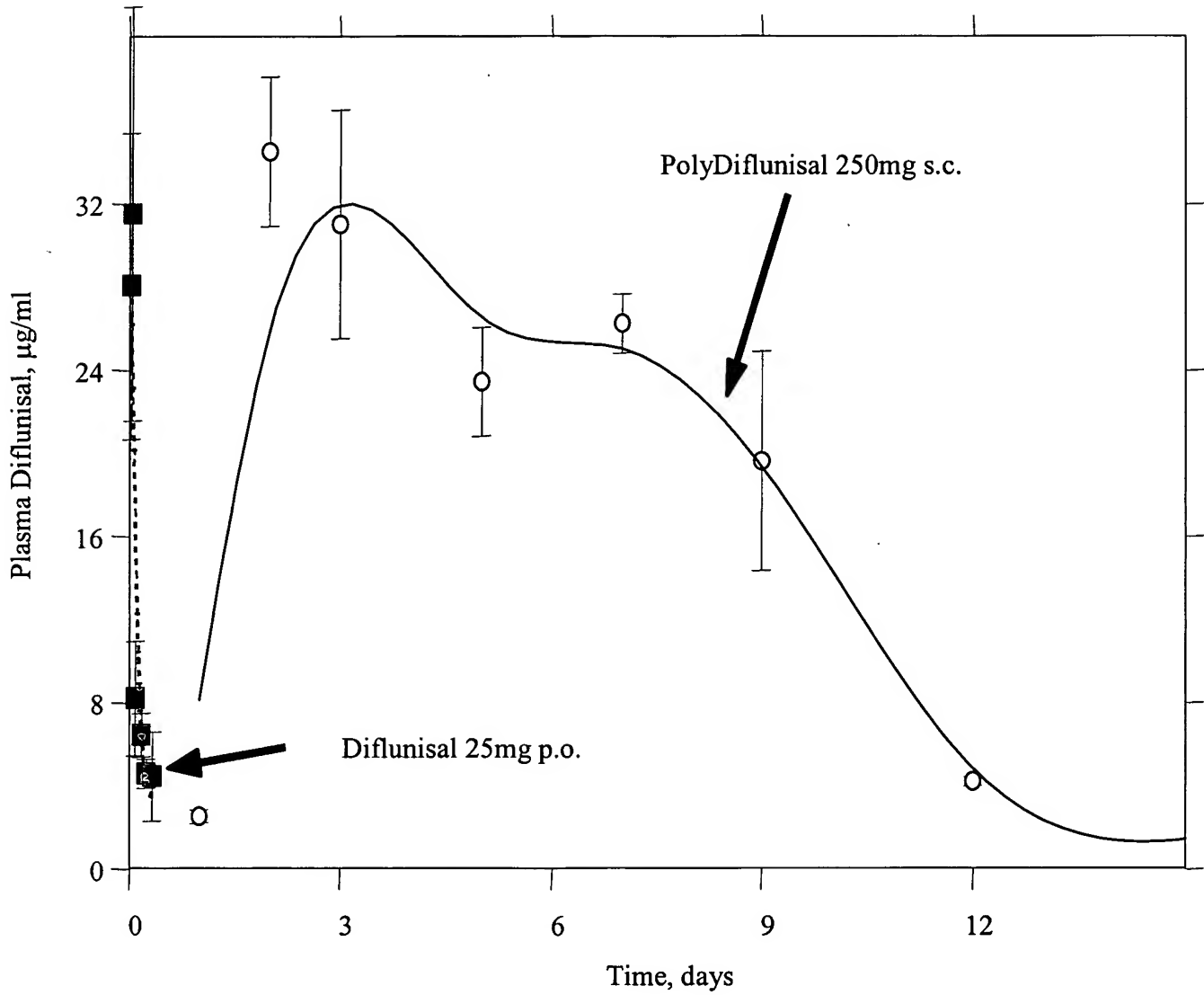


Figure 65



**Figure 66**

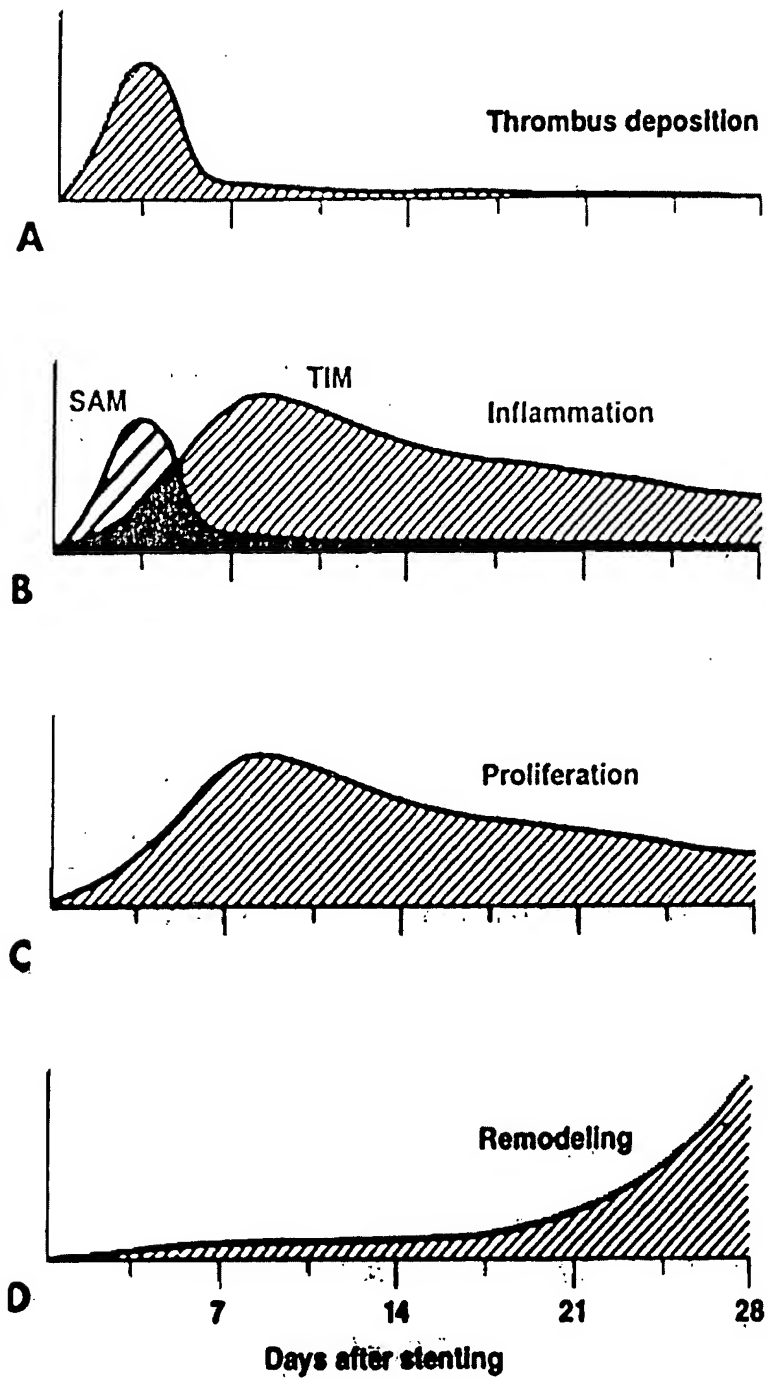
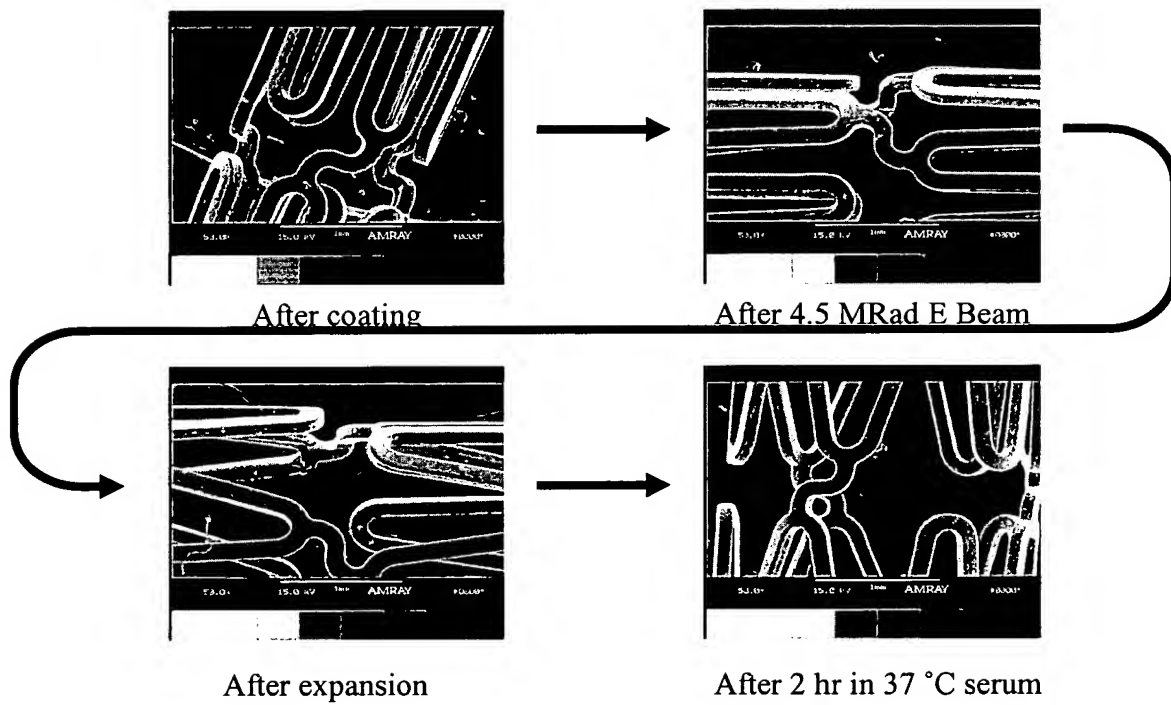
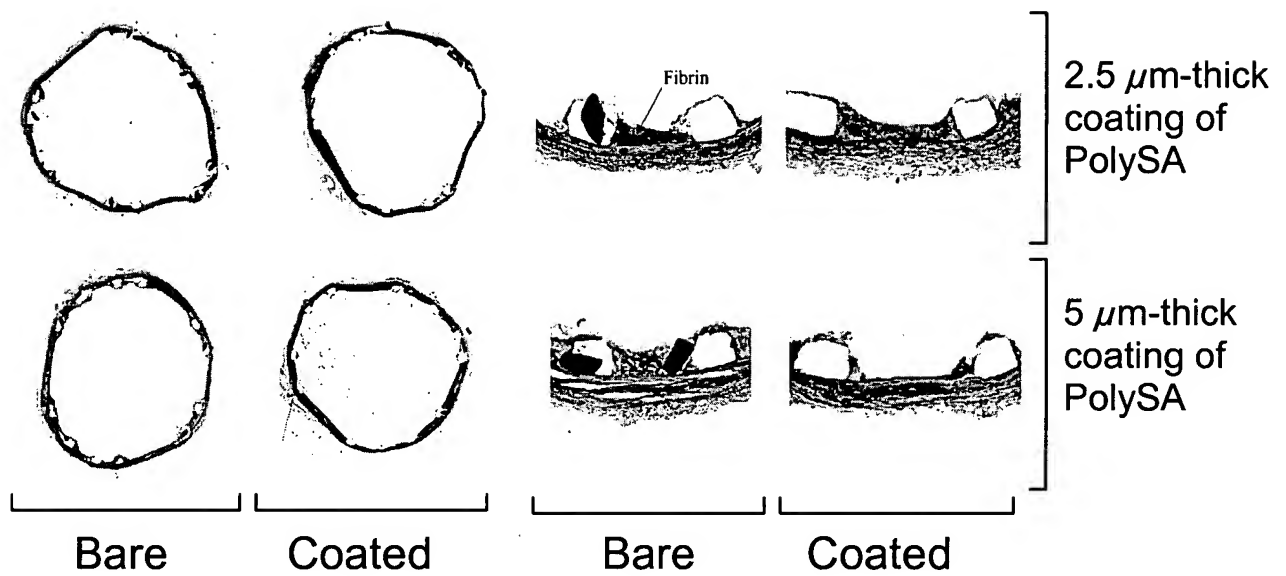


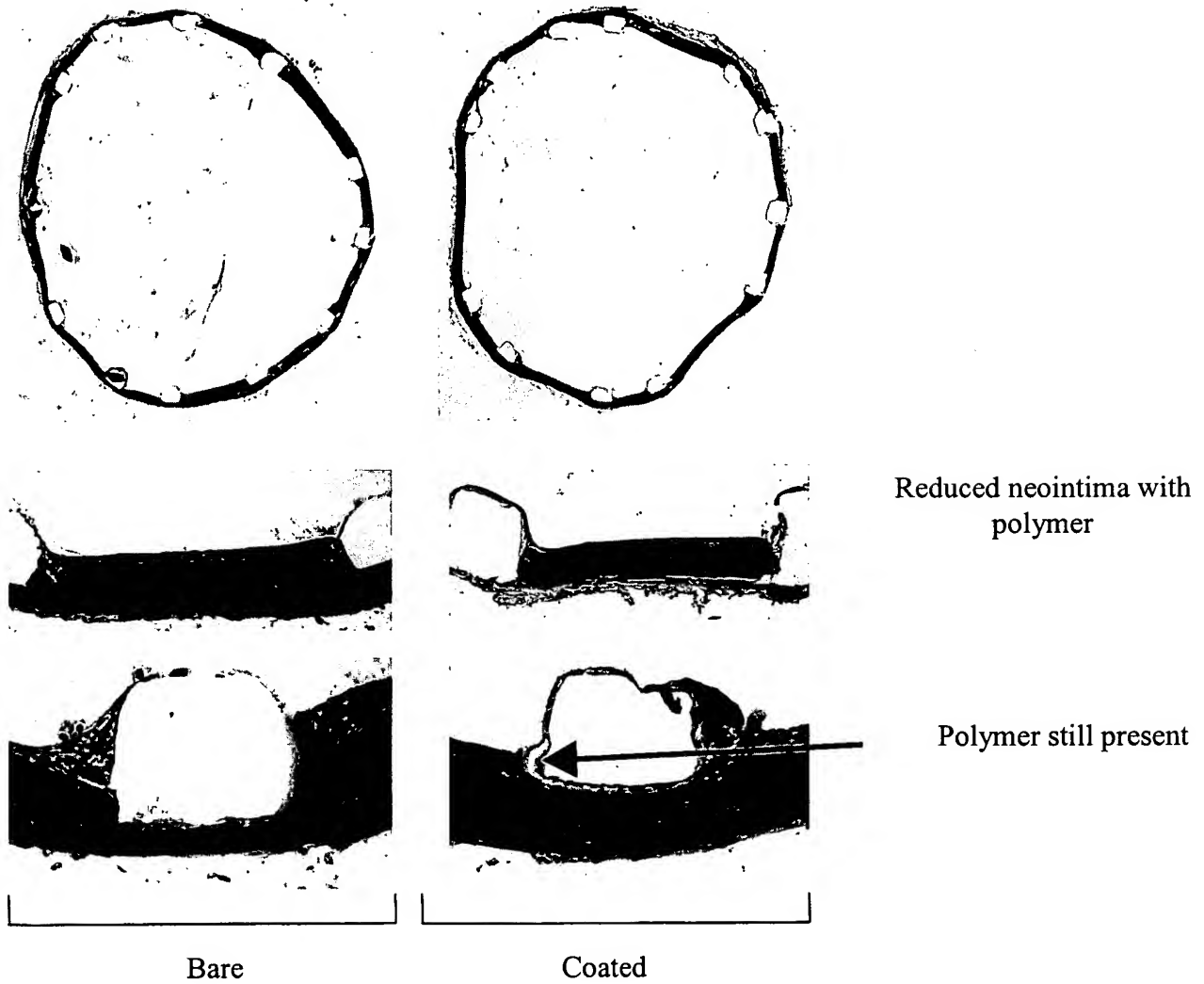
Figure 67



**Figure 68**



**Figure 69**



**Figure 70**

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